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Supplementary Material

Operationally simple regioselective 5′-phosphorylation of unprotected 5-ethynyl-2′-deoxyuridine analogues

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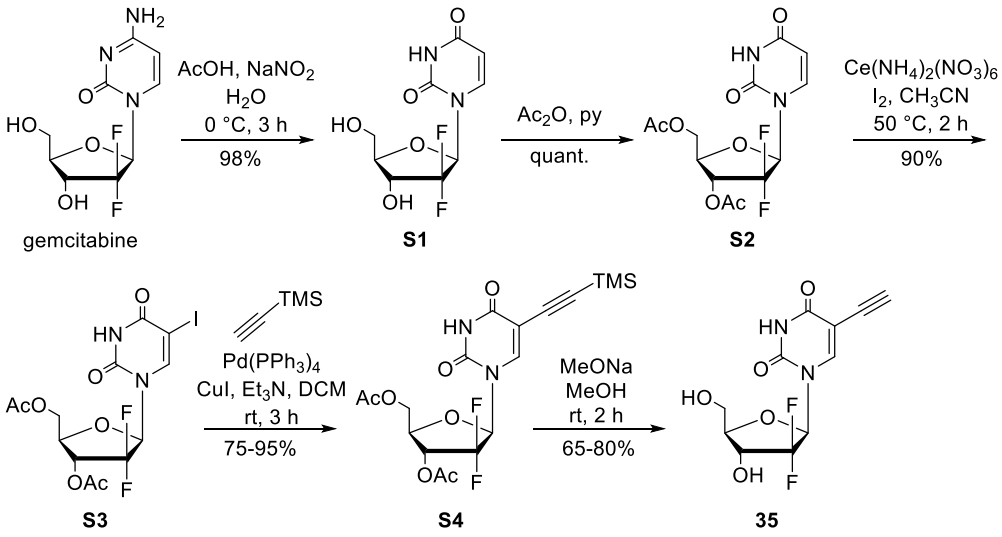
Table of Contents

Material **Page**

Fluorinated nucleosides **34** and **35** are novel and their synthesis is reported below. To the best of our knowledge, intermediate compounds **S3**, **S4** and **S8** are novel while spectroscopic data for **24** has not been reported previously.

We found that deamination of commercially available gemcitabine employing diazotisation conditions proceeded efficiently at 0 ˚C to afford 2′-dideoxy-2′-difluoro-uridine (157) in 98% yield (**Scheme S1**). Compound **S1** was subsequently acetylated with Ac_2O, employing pyridine as base and solvent, to the give the 3′,5′-protected intermediate **S2** in quantitative yield. The synthesis then follows the synthetic strategies previously developed for the synthesis of EdU. This involves iodination of the 5 position of **S2** to give **S3**, followed by Sonogashira coupling with ethynyl-2-trimethysilane to give **S4**, and lastly deprotection to afford dF-EdU (**35**) in 67% yield.



Scheme S1. Synthesis of dF-EdU (**35**) from gemcitabine.

2′-Dideoxy-2′-difluoro-uridine (**S1**)

Gemcitabine (1.00 g, 3.093 mmol) was dissolved in H_2O (1.8 mL) and AcOH (3.5 mL) and cooled to 0 ˚C. $NaNO_2$ dissolved in a minimum amount of H_2O was slowly added to the reaction mixture with stirring. The mixture was stirred for 3 h at 0 ˚C at which point TLC analysis indicated complete conversion of starting material to a single product. The mixture was allowed to warm to rt and was then poured into acetone (100 mL). The

precipitated salts were filtered off and the solvent removed *in vacuo*. The residue was co-evaporated with EtOH (2×) then the residue dissolved in MeOH and adsorbed onto silica gel. The crude product was purified by silica gel flash chromatography to afford the title compound as a clear oil (quantitative). Spectroscopic data was consistent with literature values.[1] R_f = 0.23 (10% MeOH in CH_2Cl_2). ^{1}H NMR (500 MHz, MeOD-d_4) δ_H = 7.87 (d, J = 8.2 Hz, 1H), 6.17 – 6.12 (m, 1H), 5.73 (d, J = 8.2 Hz, 1H), 4.28 (td, J = 12.1, 8.1 Hz, 1H), 3.96 – 3.87 (m, 2H), 3.78 (dd, J = 12.5, 3.1 Hz, 1H). ^{1}H NMR (500 MHz, DMSO-d_6) δ_H = 11.57 (br s, 1H, NH), 7.79 (d, J = 8.2 Hz, 1H, H-6′), 6.06 (t, J = 7.9 Hz, 1H, H-1′), 5.72 (d, J = 8.1 Hz, 1H, H-5), 4.18 (td, J = 12.8, 8.4 Hz, 1H, H-3′), 3.83 (ddd, J = 8.4, 3.6, 2.5 Hz, 1H, H-4′), 3.76 (dd, J = 12.7, 2.4 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$), 3.62 (dd, J = 12.7, 3.6 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$). ^{19}F NMR (470 MHz, MeOD-d_4) δ -118.6 (dd, J = 13.2, 4.8 Hz), -119.2 (dd, J = 13.3, 5.0 Hz), -120.0, -120.5. LRMS (ESI): *m/z* = 265 $[M + H]^+$, 263 $[M - H]^-$, 309 $[M + HCO_2]^-$.

3′,5′-*O*-Bis-acetyl-2′-dideoxy-2′-difluoro-uridine (**S2**)

Compound **S1** was dissolved in pyridine (3.3 mL, 30.93 mmol, 10 equiv) and Ac_2O (0.73 mL, 7.73 mmol, 2.5 equiv) and the mixture stirred at rt for 8 h. EtOAc (50 mL) was added and the organic material washed with 5% $HCl_{(aq)}$ (20 mL), $NaHCO_{3(satd.\ aq)}$ (20 mL), brine (20 mL) and dried over $MgSO_4$. The solvent was removed to give the title compound as a yellow gum (quantitative). R_f = 0.16 (30% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 9.40 (br s, 1H, NH), 7.36 (dd, J = 8.2, 2.4 Hz, 1H, H-6), 6.26 (dd, J = 11.9, 6.3 Hz, 1H, H-1′), 5.81 (d, J = 8.2 Hz, 1H, H-5), 5.25 (ddd, J = 13.8, 5.5, 3.0 Hz, 1H, H-3′), 4.39 (d, J = 4.2 Hz, 2H, H-5′$_{(\alpha \text{ and } \beta)}$), 4.29 (q, J = 4.4 Hz, 1H, H-4′), 2.20 (s, 3H, Ac), 2.12 (s, 3H, Ac). ^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 170.4 (H_3CCO_2), 169.1 (H_3CCO_2), 162.6 (C-4), 150.2 (C-2, 139.8 (d, J = 3.7 Hz, C-6), 120.5 (dd, J = 266.4, 259.1 Hz, C-2′), 103.4 (C-5), 83.1 (dd, J = 38.0, 20.8 Hz, C-1′), 78.0 (dd, J = 4.6, 2.5 Hz, C-4′), 70.7 (dd, J = 34.2, 17.0 Hz, C-3′), 62.1 (C-5′), 20.8 (H_3CCO_2), 20.5 (H_3CCO_2). ^{19}F NMR (470 MHz, $CDCl_3$) δ_F = -116.8 (dt, J = 247.4, 12.3 Hz), -121.4 (d, J = 250.4 Hz). LRMS (ESI): *m/z* = 349 $[M + H]^+$, 347 $[M - H]^-$. HRMS (ESI^+) *m/z* $[M + Na]^+$ calcd. for $C_{13}H_{14}F_2N_2NaO_7$ 371.0661, found 371.0634.

3′,5′-*O*-Bis-acetyl-2′-dideoxy-2′-difluoro-5-iodo-uridine (**S3**)

Compound **S3** was synthesised from compound **S2** (0.980 g, 2.815 mmol) according to adapted literature procedures.[2] The crude product was purified by silica gel flash chromatography (5 – 20% EtOAc in CH_2Cl_2) to afford the title compound as a pale yellow foam/gum (1.20 g, 90%). R_f = 0.52 (30% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.90 (br s, 1H, NH), 7.80 (d, *J* = 2.2 Hz, 1H, H-6), 6.24 (dd, *J* = 10.5, 6.9 Hz, 1H, H-1′), 5.29 (ddd, *J* = 13.3, 5.7, 3.9 Hz, 1H, H-3′), 4.42 (d, *J* = 3.5 Hz, 2H, H-5′$_{(\alpha \text{ and } \beta)}$), 4.35 – 4.29 (m, 1H, H-4′), 2.21 (2× s, 6H, Ac). ^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 170.4 (H_3CCO_2), 169.1 (H_3CCO_2), 159.3 (C-4), 149.5 (C-2), 144.1 (H-6), 120.6 (dd, *J* = 265.7, 260.0 Hz, C-2′), 83.4 (dd, *J* = 38.2, 20.7 Hz, C-1′), 78.3 (d, *J* = 2.1 Hz, H-4′), 70.5 (dd, *J* = 33.8, 17.0 Hz, H-3′), 69.4 (C-5), 61.9 (C-5′), 21.0 (H_3CCO_2), 20.5 (H_3CCO_2). ^{19}F NMR (470 MHz, $CDCl_3$) δ_F = -116.3 (dt, *J* = 247.9, 11.8 Hz), -120.6 (d, *J* = 247.7 Hz). LRMS (ESI): *m/z* = 475 $[M + H]^+$, 473 $[M - H]^-$. HRMS (ESI^+) *m/z* $[M + Na]^+$ calcd. for $C_{13}H_{13}F_2IN_2NaO_7$ 496.9628, found 496.9590.

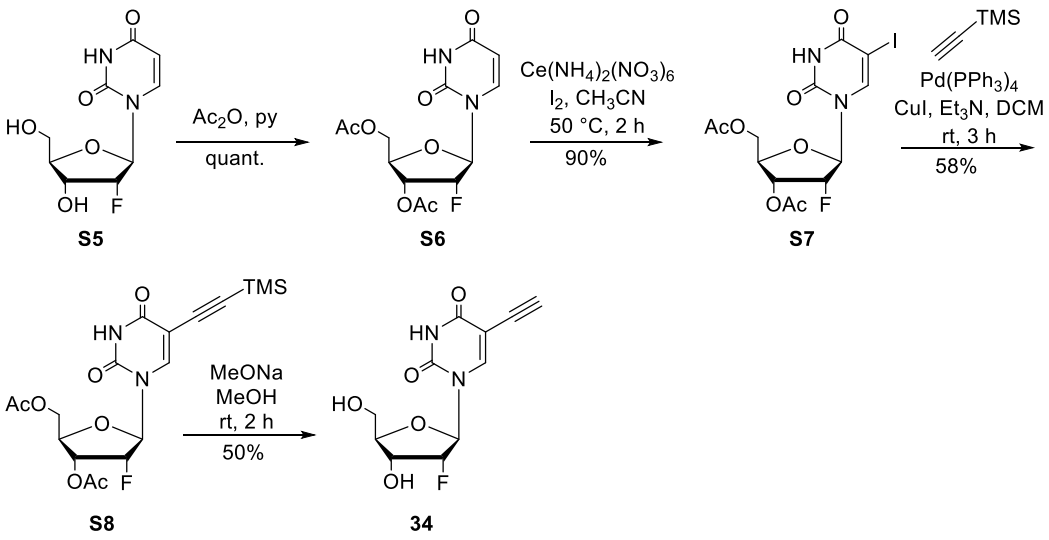
3′,5′-*O*-Bis-acetyl-2′-dideoxy-2′-difluoro-5-(ethynyl(2-trimethylsilyl))-uridine (**S4**)

Compound **S4** was synthesised from compound **S3** (1.400 g, 2.953 mmol) using Sonagashira conditions. **S3** was combined with CuI (0.056 g, 0.295 mmol, 0.1 equiv), $Pd(PPh_3)_4$ (0.154 g, 0.148 mmol, 0.05 equiv) under an atmosphere of argon. The mixture was suspended in anhydrous CH_2Cl_2 (10 mL) and ethynyl-2-trimethysilane (2 ml, 14.7 mmol, 5 equiv) added immediately, followed by Et_3N (0.8 mL, 5.9 mmol, 2 equiv). Upon addition of Et_3N the reaction mixture clarified and developed a yellow-orange colour. The mixture was stirred at rt until complete consumption of **S3** was evident by TLC (2 – 3 h). The solvent was removed *in vacuo* and the residue dissolved in EtOAc. The EtOAc fraction was washed with 5% $HCl_{(aq)}$ (20 mL), $NaHCO_{3(satd.\ aq)}$ (20 mL), 1.0 M EDTA-Na (3 × 20 mL) and brine (20 mL) then dried over $MgSO_4$ and concentrated *in vacuo.* The crude product was purified by silica gel flash chromatography (10 – 20% EtOAc in CH_2Cl_2) to afford the title compound as a colourless foam (1.246 g, 95 %). R_f = 0.66 (30% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.98 (br s, 1H, NH), 7.66 (d, *J* = 2.0 Hz, 1H, H-6), 6.26 (t, *J* = 8.4 Hz, 1H, H-1′), 5.31 (dt, *J* = 12.9, 5.8 Hz, 1H, H-3′), 4.44 (dd, *J* = 12.7, 3.1 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$), 4.38 (dd, *J* = 12.7, 3.5 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$), 4.31 (dt, *J* = 6.4, 3.3 Hz, 1H, H-4′), 2.20 (s, 3H, Ac), 2.18 (s, 3H, Ac), 0.22 (s, 9H, $Si(CH_3)_3$). ^{13}C

NMR (126 MHz, $CDCl_3$) δ_C = 170.2 (H_3CCO_2), 169.1 (H_3CCO_2), 160.3, 148.9 (C-2), 142.4 (d, *J* = 2.7 Hz, C-6), 120.6 (dd, *J* = 264.4, 261.3 Hz, C-2′), 101.5 (C-5), 100.6 (C≡C), 94.6 (C≡C), 83.7 (dd, *J* = 39.5, 21.6 Hz, C-1′), 78.0 (d, *J* = 5.6 Hz, C-4′), 70.3 (dd, *J* = 32.9, 17.0 Hz, C-3′) 61.8 (C-5′), 20.9 (H_3CCO_2), 20.5 (H_3CCO_2), -0.1 ($Si(CH_3)_3$). ^{19}F NMR (470 MHz, $CDCl_3$) δ_F = -115.9 (dt, *J* = 247.6, 10.8 Hz), -119.6 (d, *J* = 249.6 Hz). LRMS (ESI): *m/z* = 445 $[M + H]^+$, 443 $[M - H]^-$. HRMS (ESI^+) *m/z* $[M + Na]^+$ calcd. for $C_{18}H_{22}F_2N_2NaO_7Si$ 467.1057, found 467.1018.

2′-dideoxy-2′-difluoro-5-ethynyl-uridine (**35**)

Compound **S4** (0.466 g, 1.049 mmol) was dissolved in MeOH (15 mL) and sodium methoxide (4.6 M) (0.187 mL, 0.0404 mmol) added. The mixture was stirred at rt for 3 hours after which TLC analysis indicated complete consumption of the starting material and formation of a single product. The mixture was neutralised with Amberlite IRA-120 H^+ resin and filtered. The crude compound was adsorbed onto silica and purified by solid addition silica gel flash chromatography (10 % MeOH in CH_2Cl_2) to afford the title compound as a pale yellow solid (0.257 g, 85%). Spectroscopic data was consistent with literature.[1] R_f = 0.11 (5% MeOH in CH_2Cl_2). Darkens at 190-205 ˚C, mp = 210-215 ˚C. ^1H NMR (500 MHz, DMSO) δ_H = 11.91 (br s, 1H, NH), 8.26 (s, 1H, H-6), 6.32 (d, *J* = 6.6 Hz, 1H, OH-3′), 6.04 (t, *J* = 7.3 Hz, 1H, H-1′), 5.42 (t, *J* = 5.2 Hz, 1H, OH-5′), 4.22 (tdd, *J* = 12.4, 10.6, 8.3, 5.6 Hz, 1H, H-3′), 4.17 (s, 1H), 3.86 (dt, *J* = 8.6, 2.7 Hz, 1H, H-4′), 3.79 (dt, *J* = 12.8, 3.0 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$), 3.64 (ddd, *J* = 12.7, 5.4, 3.1 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$). ^{19}F NMR (470 MHz, DMSO) δ_F = -116.3, -116.5 (d, *J* = 12.3 Hz), -116.83 (d, *J* = 13.5 Hz), -117.00 (d, *J* = 13.1 Hz), -117.18, -117.70. LRMS (ESI): *m/z* = 289 $[M + H]^+$, 287 $[M - H]^-$.



Scheme S2. Synthesis of 2′-F-*ribo*-EdU (**34**) from commercially available 2′-deoxy-2′-fluoro-deoxyuridine (**S5**) employing an adapted procedure for the synthesis of EdU.

(2′*R*)-3′,5′-*O*-Bis-acetyl-2′-deoxy-2′-fluoro-uridine (**S6**)

Compound **S6** was synthesised from commercially available (2′*R*)-2′-deoxy-2′-fluoro-uridine (**S5**) (2.000 g, 8.127 mmol). Compound **S5** was dissolved in pyridine (8.8 mL, 81.0 mmol, 10 equiv) then Ac_2O (1.92 mL, 20.3 mmol, 2.5 mmol) was added and mixture stirred for at rt 16 h. The reaction mixture was dissolved in EtOAc (50 mL) and washed with 5% $HCl_{(aq)}$ (20 mL), $NaHCO_{3(satd.\ aq)}$ (20 mL), brine (20 mL) and dried over $MgSO_4$ to give the title compound as a yellow gum (2.623 g, 98%). The spectroscopic data was consistent with literature values.[2-3] R_f = 0.21 (30% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ_H = 11.47 (s, 1H, NH), 7.72 (d, *J* = 8.1 Hz, 1H, H-6), 5.87 (dd, *J* = 22.4, 2.1 Hz, 1H, H-1′), 5.68 (d, *J* = 8.0 Hz, 1H, H-5), 5.53 (ddd, *J* = 52.6, 5.3, 2.1 Hz, 1H, H-2′), 5.26 (ddd, *J* = 17.2, 7.9, 5.3 Hz, 1H, H-3′), 4.34 (dd, *J* = 12.1, 2.9 Hz, 1H, H-5′$_{(\alpha\ or\ \beta)}$), 4.27 (ddd, *J* = 8.2, 5.7, 2.9 Hz, 1H, H-4′), 4.16 (dd, *J* = 12.1, 5.7 Hz, 1H, H-5′$_{(\alpha\ or\ \beta)}$), 2.11 (s, 3H, Ac), 2.04 (s, 3H, Ac). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 9.30 (br s, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 5.83 – 5.74 (m, 2H), 5.37 (ddd, *J* = 52.2, 4.9, 1.7 Hz, 1H), 5.15 (ddd, *J* = 17.8, 8.3, 5.0 Hz, 1H), 4.44 (dd, *J* = 12.3, 2.6 Hz, 1H), 4.40 (ddd, *J* = 7.6, 4.5, 2.6 Hz, 1H), 4.30 (dd, *J* = 12.3, 4.6 Hz, 1H), 2.15 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 170.1, 169.5, 150.6, 142.5, 102.1, 90.8 (d, *J* = 187.0 Hz), 90.5 (d, *J* =

36.4 Hz), 77.9, 69.8 (d, J = 14.8 Hz), 62.67, 20.5, 20.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ -198.76 – -199.06 (m). LRMS (ESI): m/z = 353 $[M + Na]^+$, 331 $[M + H]^+$, 329 $[M - H]^-$.

(2′*R*)-3′,5′-*O*-Bis-acetyl-2′-deoxy-2′-fluoro-5-iodo-uridine (**S7**)

Compound **S7** was synthesised from compound **S6** (2.68 g, 8.11 mmol) according to literature procedures.[2] Briefly, compound **S6**, ceric ammonium nitrate (4.45 g, 8.11 mmol, 1 equiv), and I_2 (1.64 g, 6.49 mmol 0.8 equiv) were combined and dissolved in CH_3CN (40 mL) and heated to 50 °C for 16 h. The solvent was then removed *in vacuo* and the residue dissolved in EtOAc (20 mL) and washed with $NaHCO_{3(satd.\ aq.)}$ (20 mL) and brine (20 mL) then dried over $MgSO_4$. The crude product was purified by silica gel flash chromatography (10 – 30% EtOAc in CH_2Cl_2) to afford the title compound as a pale red solid (3.330 g, 90%). R_f = 0.52 (30% EtOAc in CH_2Cl_2). mp 135-140 ˚C. The spectroscopic data was consistent with literature values.[3] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H, NH), 7.89 (s, 1H, H-6), 5.89 (dd, J = 18.2, 1.7 Hz, 1H, H-1′), 5.30 (ddd, J = 51.7, 4.7, 1.7 Hz, 1H, H-2′), 5.10 (ddd, J = 18.1, 8.0, 4.8 Hz, 1H, H-3′), 4.49 – 4.41 (m, 2H, H-5′$_{(\alpha\ or\ \beta)}$ and H-4′), 4.36 (dd, J = 13.2, 4.0 Hz, 1H, H-5′$_{(\alpha\ or\ \beta)}$), 2.22 (s, 3H, Ac), 2.16 (s, 3H, Ac). ^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 170.5 (H_3CCO_2), 170.0 (H_3CCO_2), 160.0 (C-4), 149.6 (C-2), 144.5 (C-6), 91.1 (d, J = 193.0 Hz, C-2′), 90.3 (d, J = 35.6 Hz, C-1′), 78.9 (C-4′, 69.3 (d, J = 15.6 Hz, C-3′), 61.9 (C-5′), 21.3 (H_3CCO_2), 20.5 (H_3CCO_2). ^{19}F NMR (470 MHz, $CDCl_3$) δ -200.2 (dt, J = 51.9, 18.2 Hz). LRMS (ESI): m/z = 457 $[M + H]^+$, 455 $[M - H]^-$.

(2′*R*)-3′,5′-*O*-Bis-acetyl-2′-deoxy-5-(ethynyl(2-trimethylsilyl))-2′-fluoro-uridine (**S8**)

Compound **S8** was synthesised from compound **S7** (1.700 g, 3.728 mmol) under Sonagashira conditions, similarly to **S4** described above. The crude product was purified by silica gel flash chromatography (10 – 20% EtOAc in CH_2Cl_2) to afford the title compound as an off-white solid (0.921 g, 58%). mp 195-198 ˚C. R_f = 0.69 (30% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.74 (s, 1H, NH), 7.79 (s, 1H, H-6), 5.95 (dd, J = 17.6, 1.5 Hz, 1H, H-1′), 5.26 (ddd, J = 51.6, 4.7, 1.5 Hz, 1H, H-2′), 5.07 (ddd, J = 18.9, 8.4, 4.7 Hz, 1H, H-3′), 4.49 – 4.43 (m, 2H, H-5′$_{(\alpha\ or\ \beta)}$ and H-4′), 4.38 – 4.31 (m, 1H, H-5′$_{(\alpha\ or\ \beta)}$), 2.19 (s, 3H, Ac), 2.16 (s, 3H, Ac), 0.21 (s, 9H, $Si(CH_3)_3$). ^{13}C NMR (126

MHz, $CDCl_3$) δ_C = 170.2 (H_3CCO_2), 170.0 (H_3CCO_2), 160.6 (C-4), 148.7 (C-2), 142.5 (C-6), 101.1 (C≡*C*-Si), 100.6 (C-5), 94.8 (*C*≡C-Si), 91.2 (d, *J* = 193.4 Hz, C-2′), 89.9 (d, *J* = 35.3 Hz, C-1′), 78.8, 69.1 (d, *J* = 15.7 Hz, C-3′), 61.6 (C-5′), 21.1 (H_3CCO_2), 20.5 (H_3CCO_2), -0.1 ($Si(CH_3)_3$. ^{19}F NMR (470 MHz, $CDCl_3$) δ_F = -201.4 (dt, *J* = 51.8, 18.2 Hz). LRMS (ESI): *m/z* = 427 $[M + H]^+$, 425 $[M - H]^-$. HRMS (ESI^+) *m/z* $[M + Na]^+$ calcd. for $C_{18}H_{23}FN_2NaO_7Si$ 449.1151, found 449.1122.

(2′*R*)-2′-Deoxy-5-ethynyl-2′-fluoro-uridine (**34**)

Compound **S8** (0.880 g, 1.049 mmol) was dissolved in MeOH (30 mL) and sodium methoxide (4.6 M) (0.368 mL, 1.70 mmol) added. The mixture was stirred at rt for 2 h after which TLC analysis indicated complete consumption of the starting material and formation of a single product. The mixture was neutralised with Amberlite IRA-120 H^+ resin and filtered. Silica gel was added to the filtrate and the solvent removed *in vacuo*. The compound was purified by solid addition silica gel flash chromatography (10% MeOH in CH_2Cl_2) to afford the title compound as an off-white foam (0.280 g, 50%). R_f = 0.27 (10% MeOH in CH_2Cl_2). ^1H NMR (500 MHz, DMSO-d_6) δ_H = 11.69 (br s, 1H, NH), 8.41 (s, 1H, H-6), 5.86 (dd, *J* = 16.9, 1.3 Hz, 1H, H-1′), 5.60 (d, *J* = 6.6 Hz, 1H, OH-3′), 5.36 (t, *J* = 4.7 Hz, 1H, OH-5′), 5.03 (ddd, *J* = 53.1, 4.3, 1.4 Hz, 1H, H-1′), 4.24 – 4.11 (m, 1H, H-3′), 4.08 (s, 1H, ≡C-H), 3.89 (dt, *J* = 8.3, 2.5 Hz, 1H, H-4′), 3.81 (ddd, *J* = 12.4, 4.4, 2.3 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$), 3.60 (ddd, *J* = 12.3, 4.4, 2.5 Hz, 1H, H-5′$_{(\alpha \text{ or } \beta)}$). ^{13}C NMR (126 MHz, DMSO-d_6) δ_C = 162.0 (C-4), 149.5 (C-2), 144.5 (C-6), 97.6 (C-5), 93.9 (d, *J* = 185.3 Hz, C-2′), 87.7 (d, *J* = 34.2 Hz, C-1′), 83.7 (C≡*C*-H), 83.2 (C-4′), 76.5 (*C*≡C-H), 66.9 (d, *J* = 16.3 Hz, C-3′), 58.7 (C-5′). ^{19}F NMR (470 MHz, DMSO-d_6) δ δ -202.5 (ddd, *J* = 53.0, 23.5, 16.8 Hz). LRMS (ESI): *m/z* = 293 $[M + Na]^+$, 271 $[M + H]^+$, 269 $[M - H]^-$. HRMS (ESI^+) *m/z* $[M + Na]^+$ calcd. for $C_{11}H_{11}FN_2NaO_5$ 293.0544, found 293.0542.

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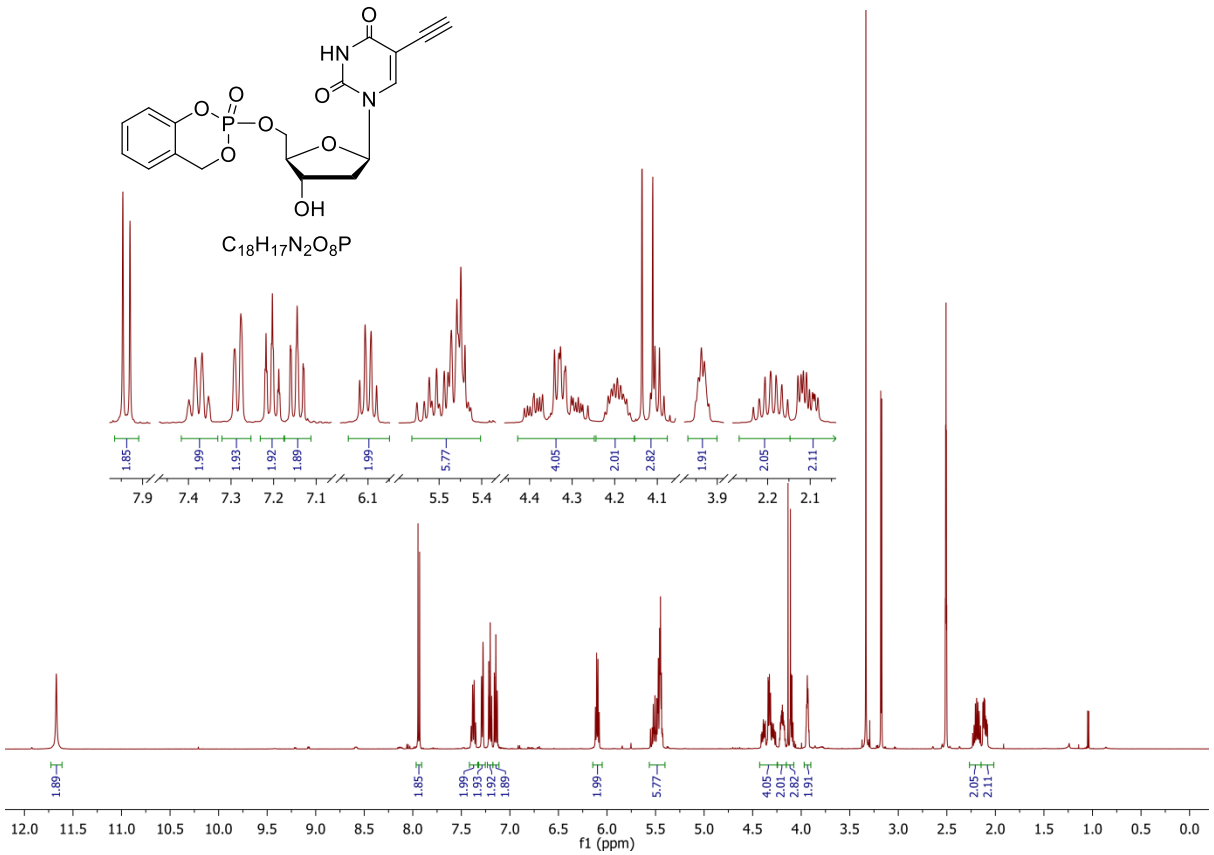
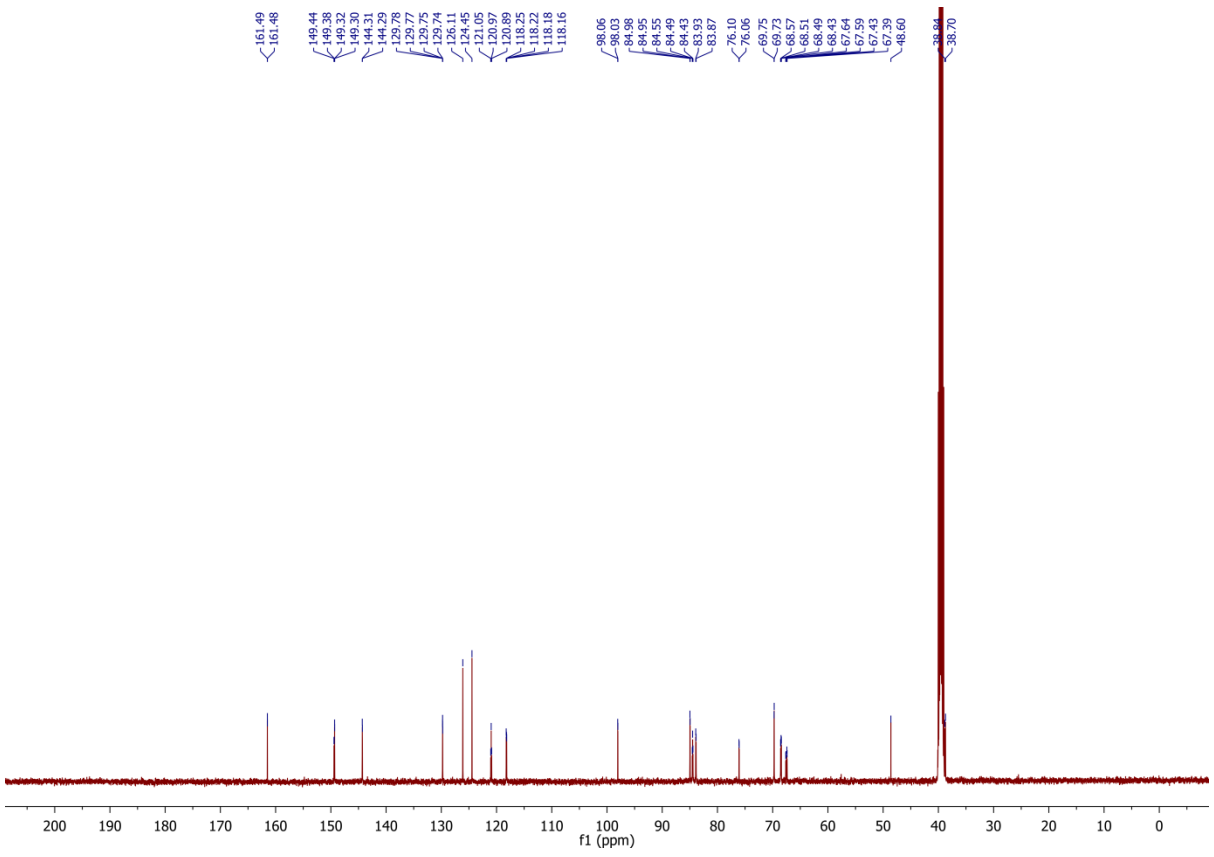
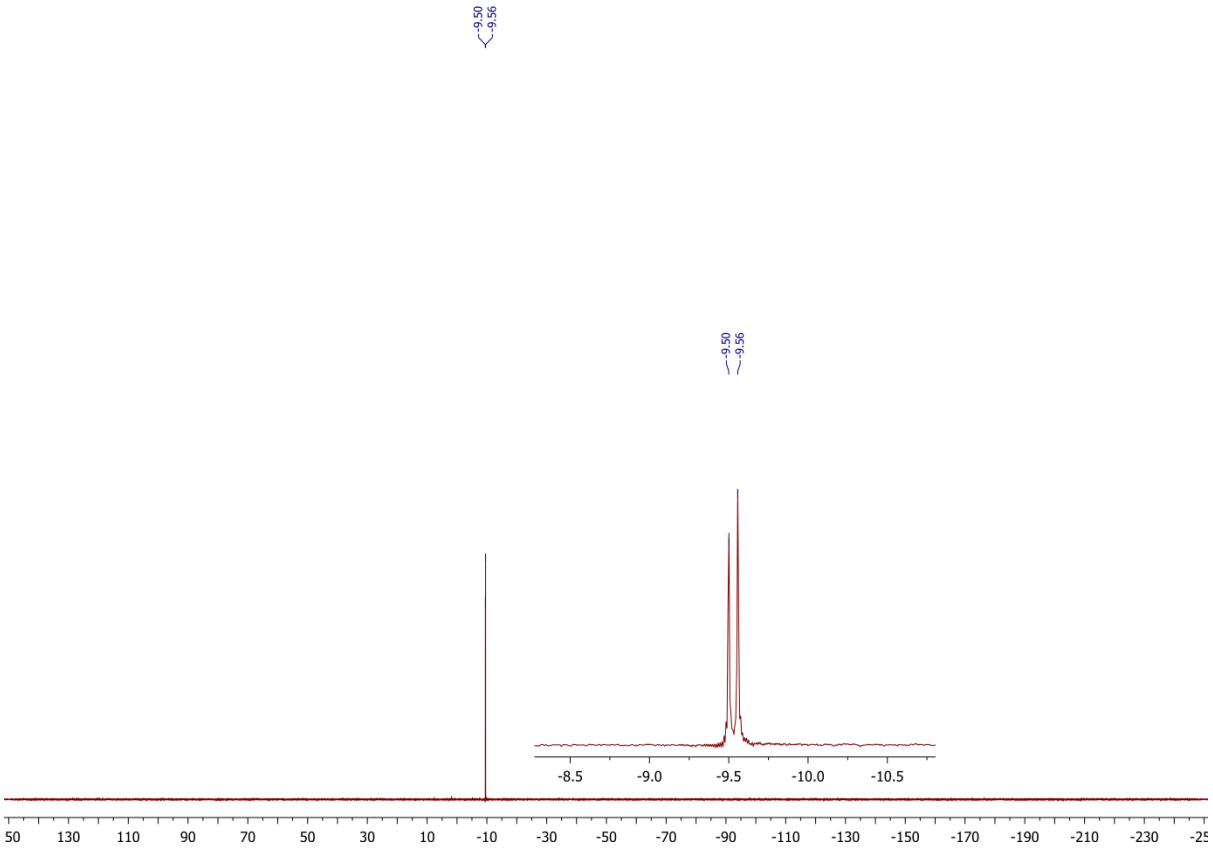
Compound **2** ^{1}H and ^{13}C NMR (DMSO-d_6)

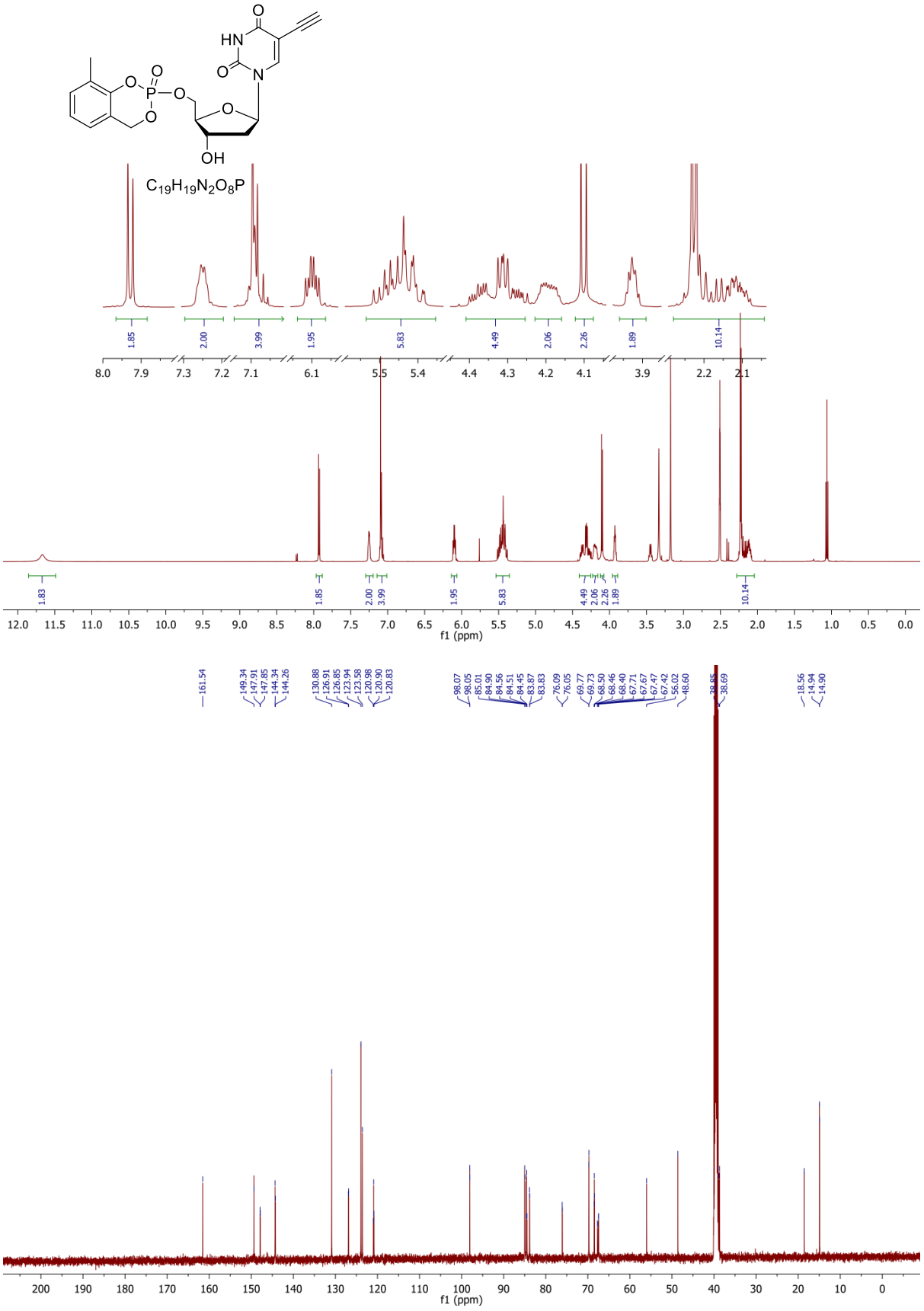




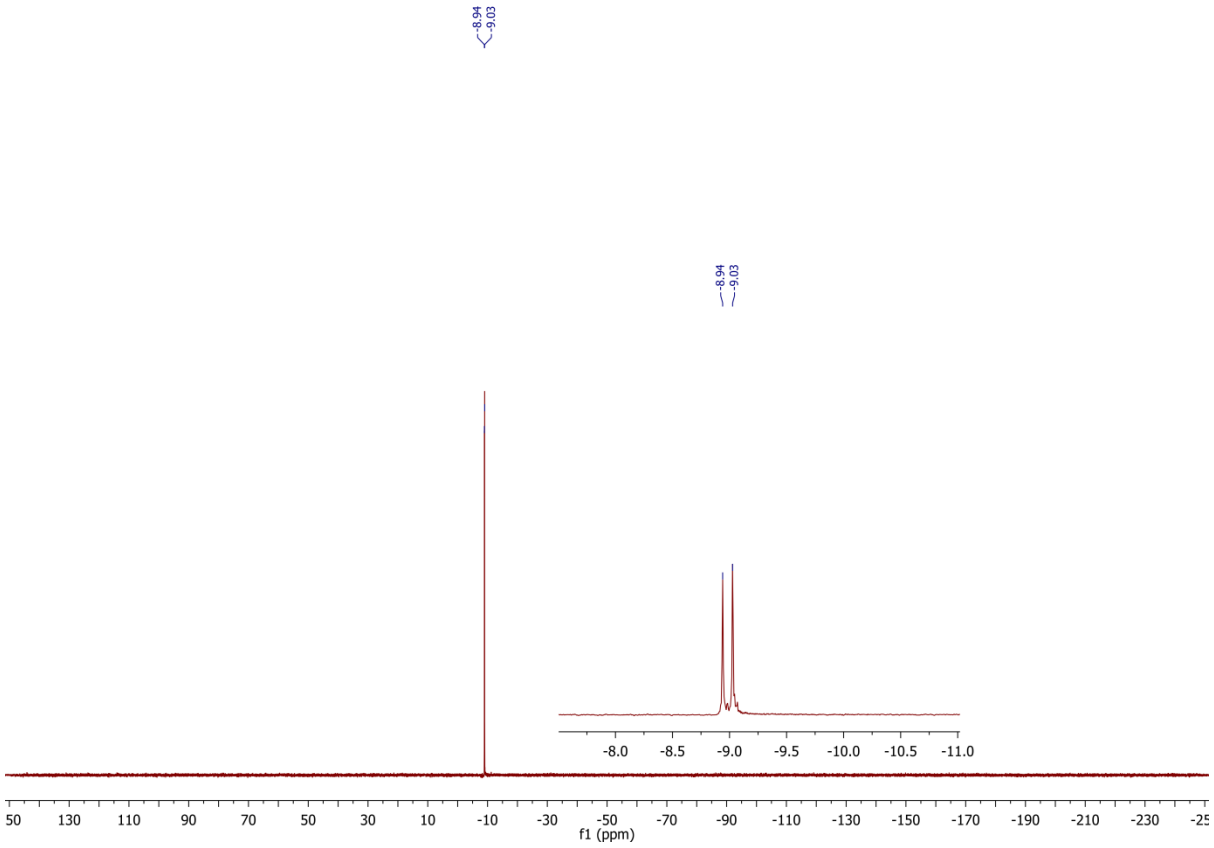
Compound **2** $^{31}P\{H\}$ NMR (DMSO-d_6)



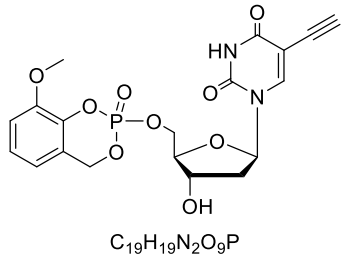
Compound **4** ^{1}H and ^{13}C NMR (DMSO-d_6)



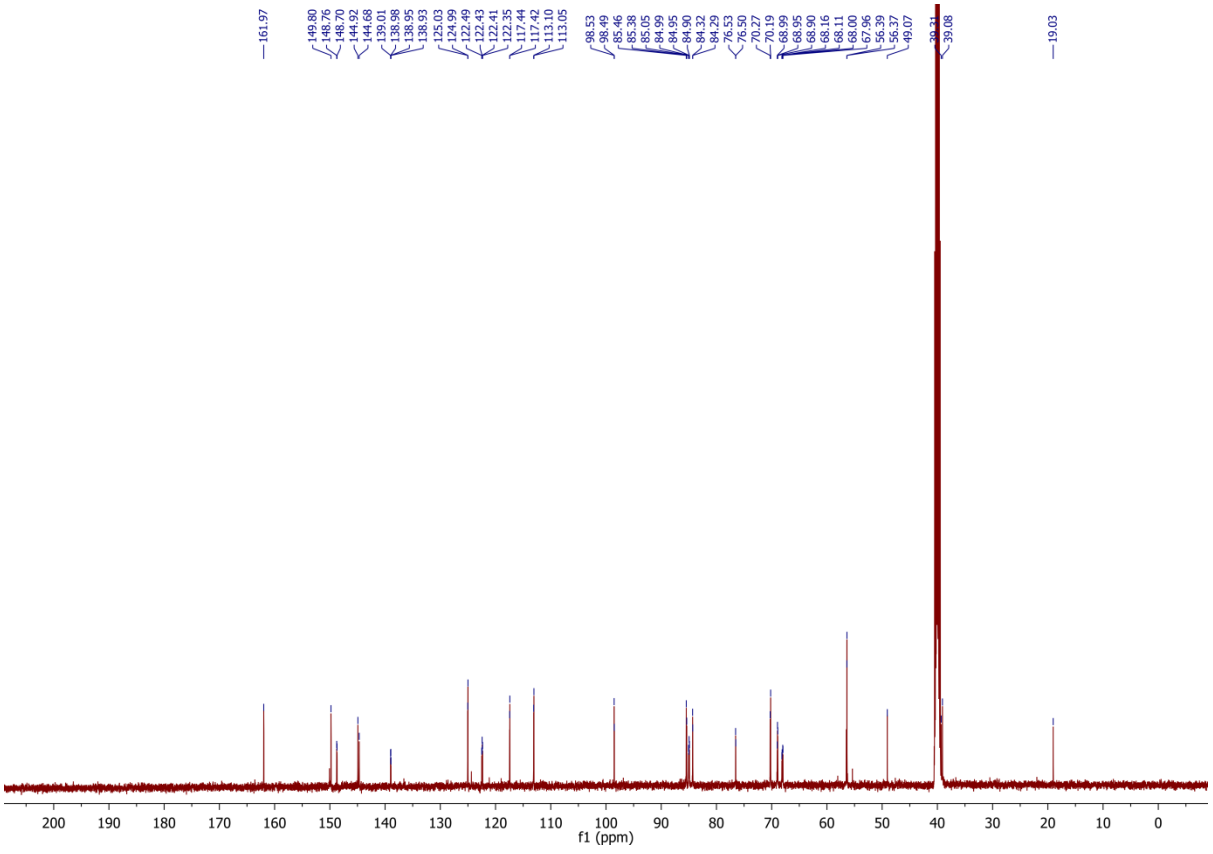
Compound **4** $^{31}P\{H\}$ NMR (DMSO-d_6)



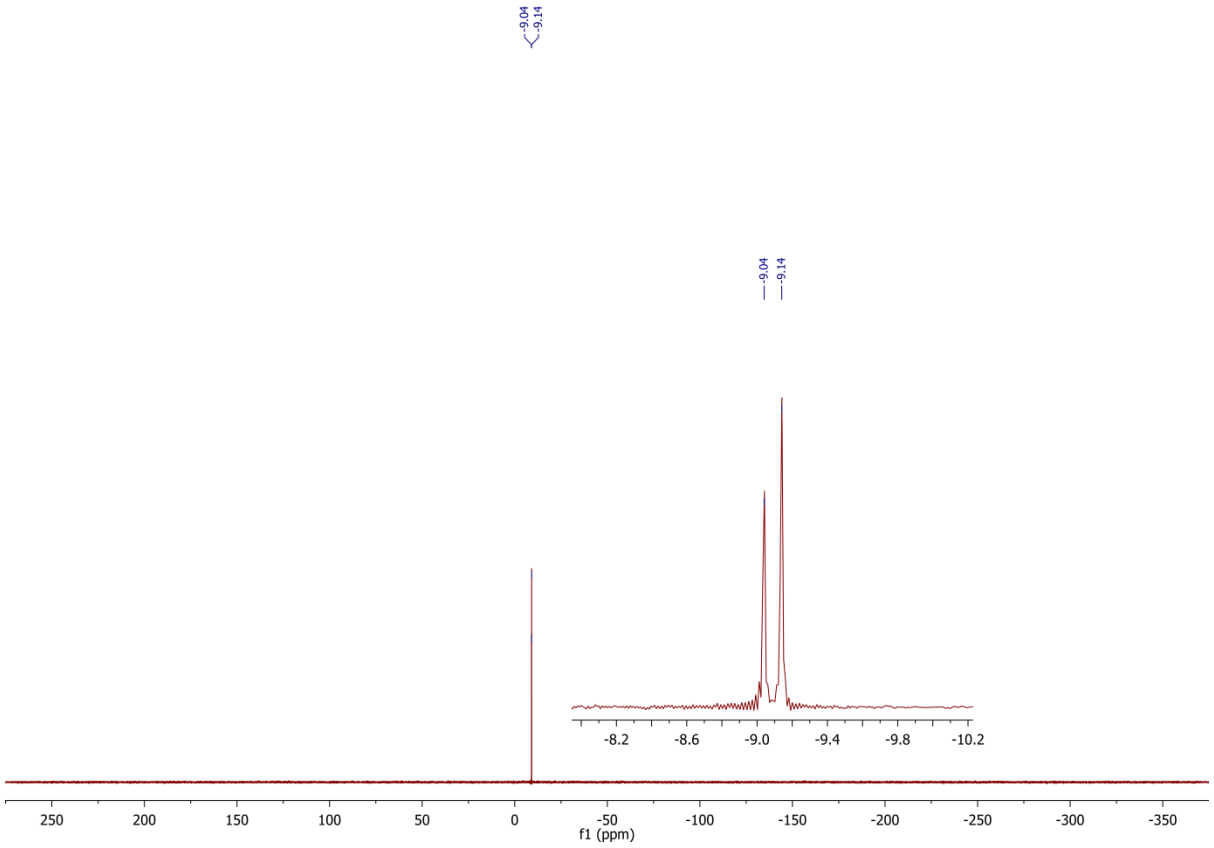
Compound **5** ^{1}H and ^{13}C NMR (DMSO-d_6)



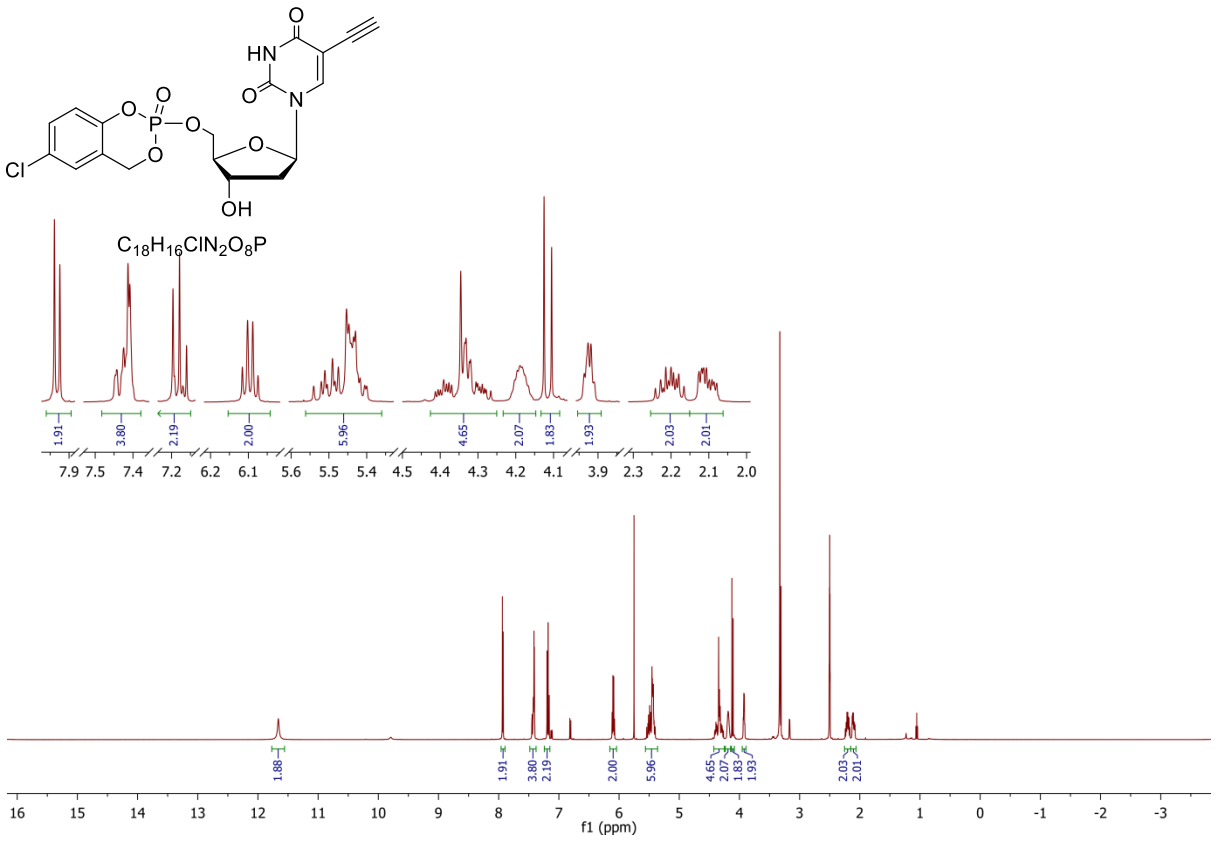
$C_{19}H_{19}N_2O_9P$

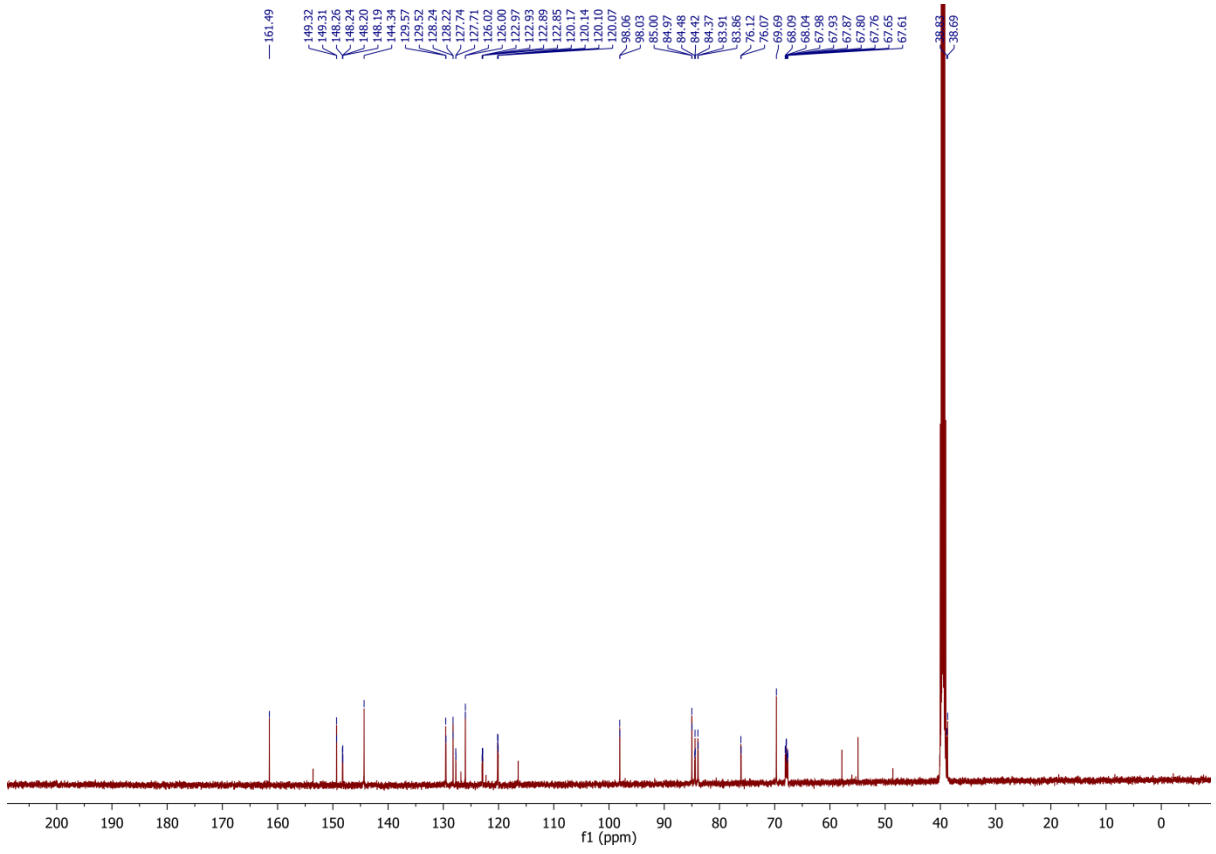


Compound **5** $^{31}P\{H\}$ NMR (DMSO-d_6)

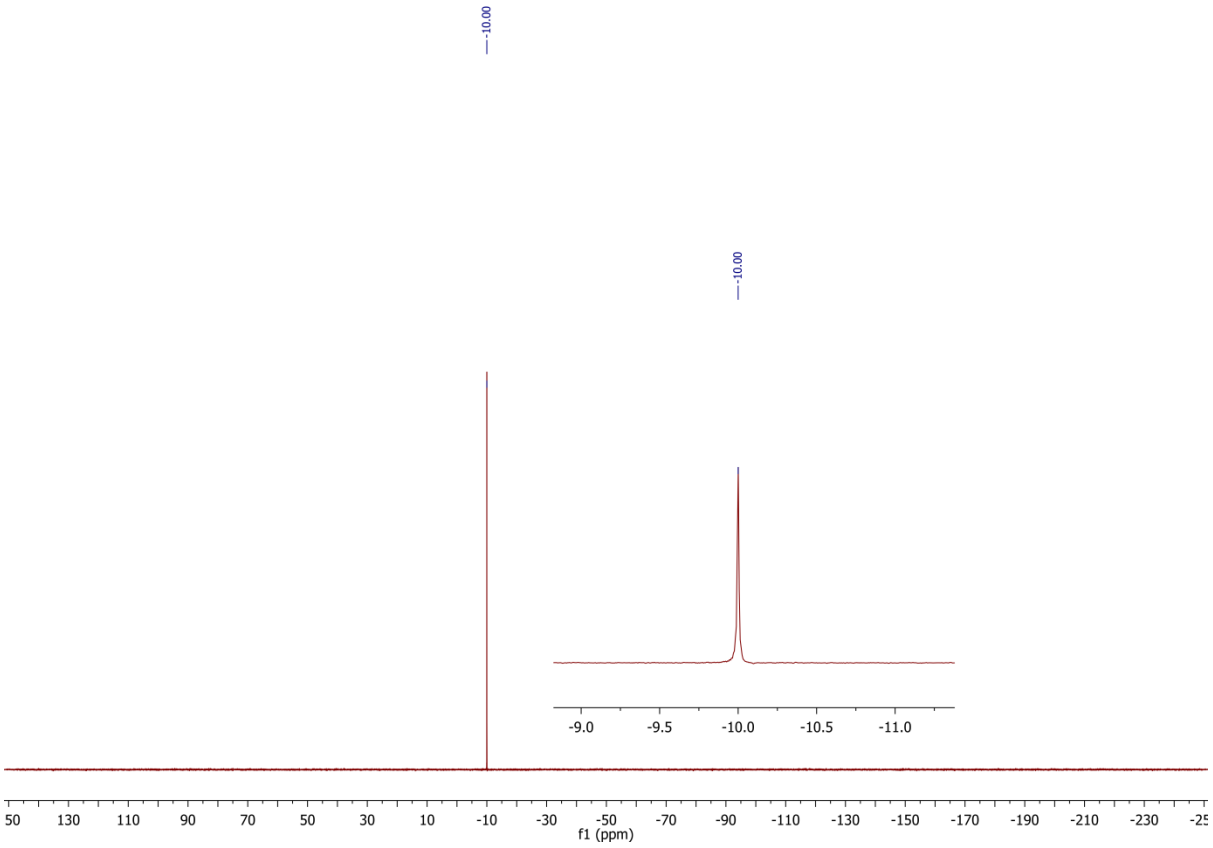


Compound **6** ^{1}H and ^{13}C NMR (DMSO-d_6)

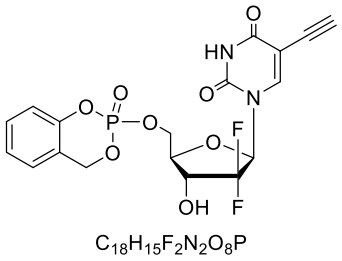




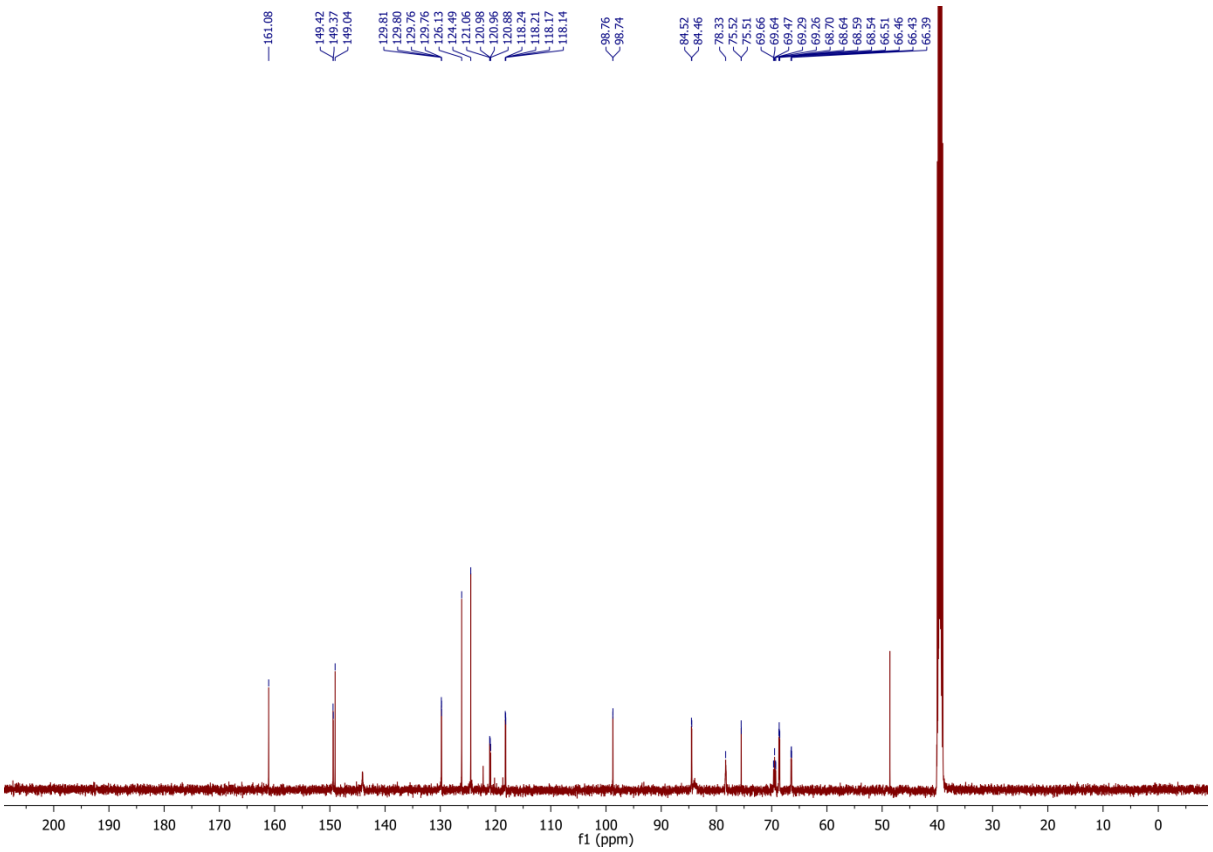
Compound **6** $^{31}P\{H\}$ NMR (DMSO-d_6)



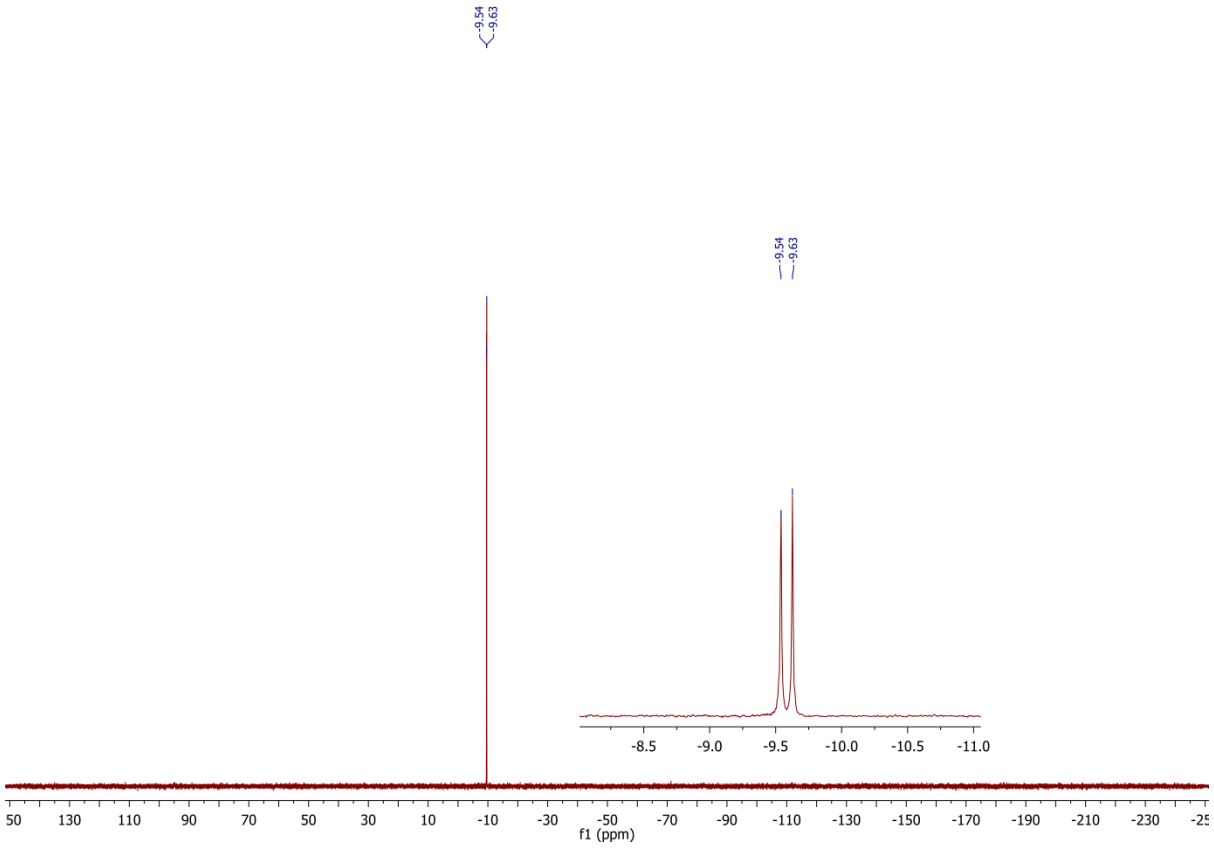
Compound **7** ^{1}H and ^{13}C NMR (DMSO-d_6)



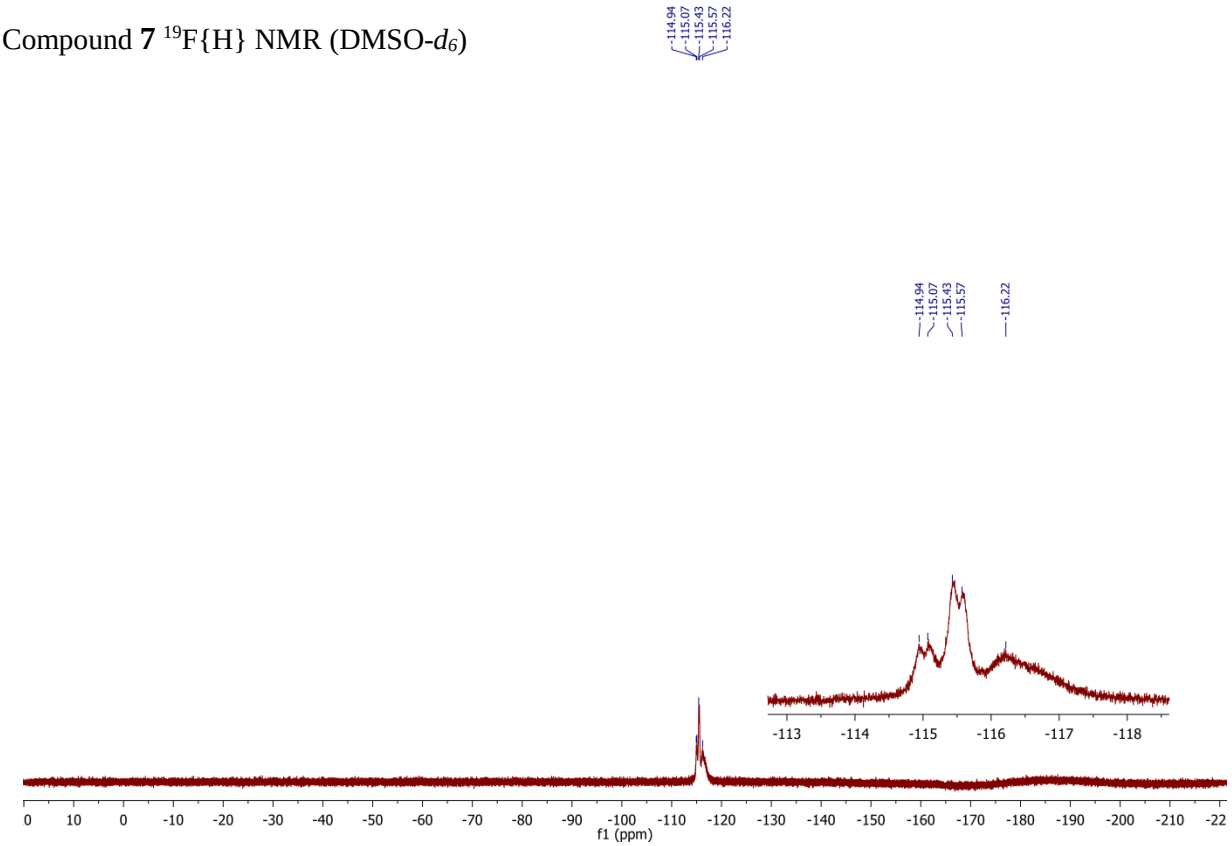
$C_{18}H_{15}F_2N_2O_8P$



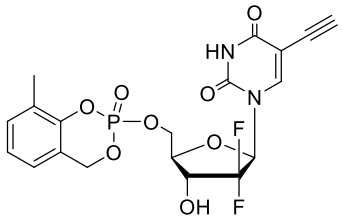
Compound **7** $^{31}P\{H\}$ NMR (DMSO-d_6)



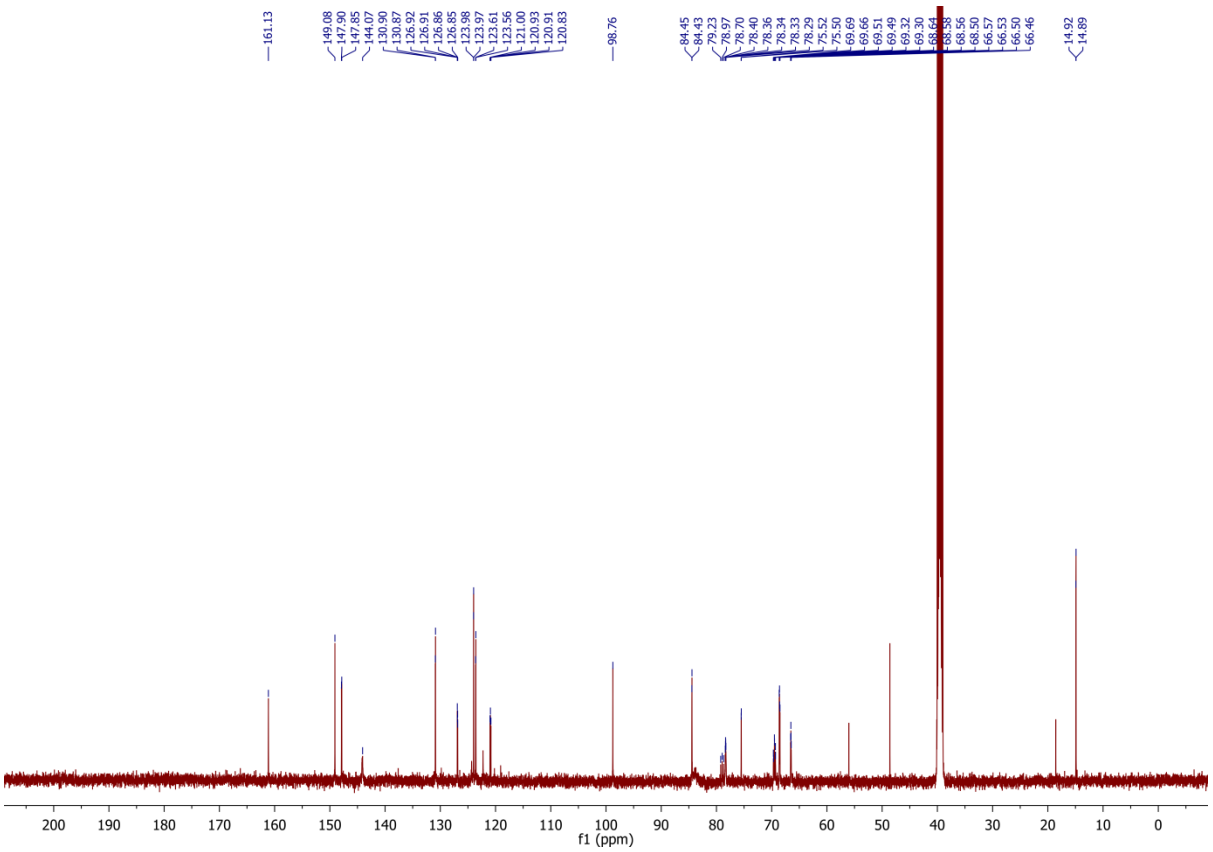
Compound **7** $^{19}F\{H\}$ NMR (DMSO-d_6)



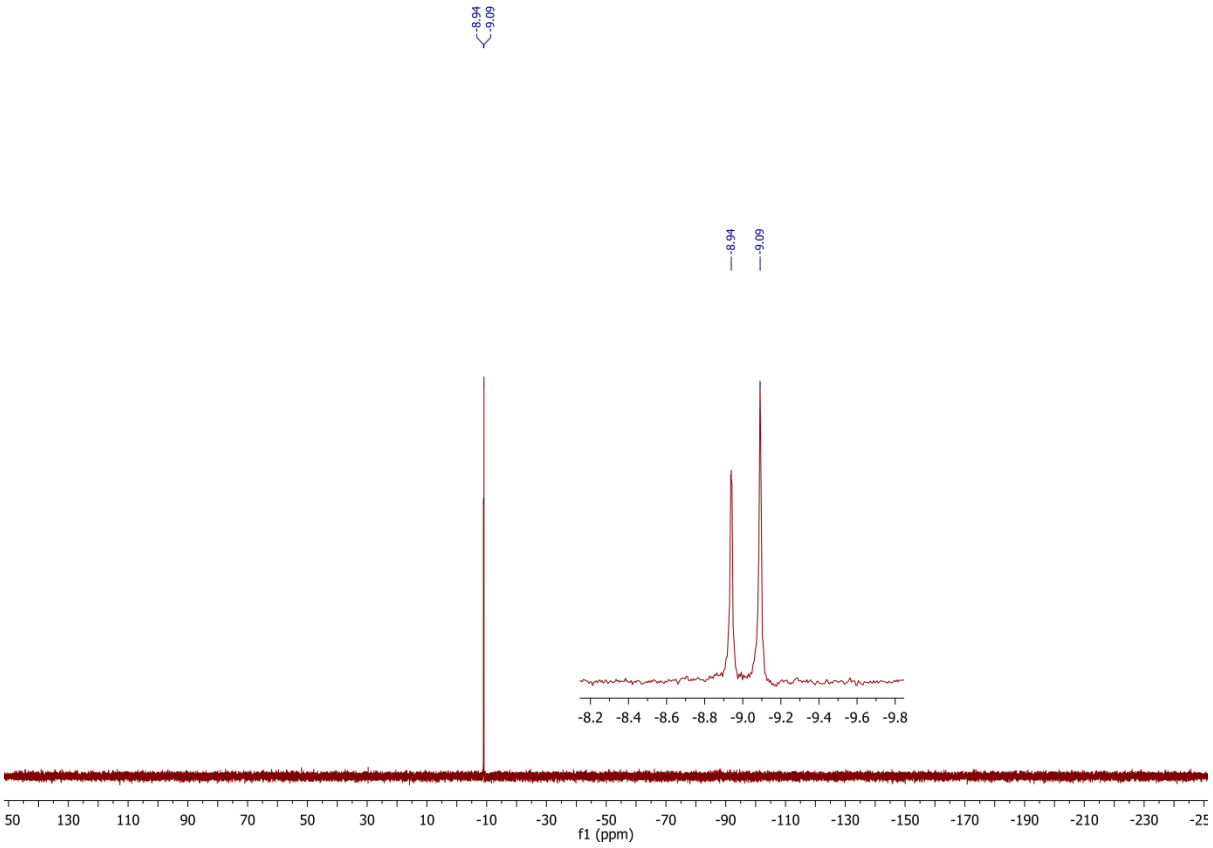
Compound **8** ^{1}H and ^{13}C NMR (DMSO-d_6)



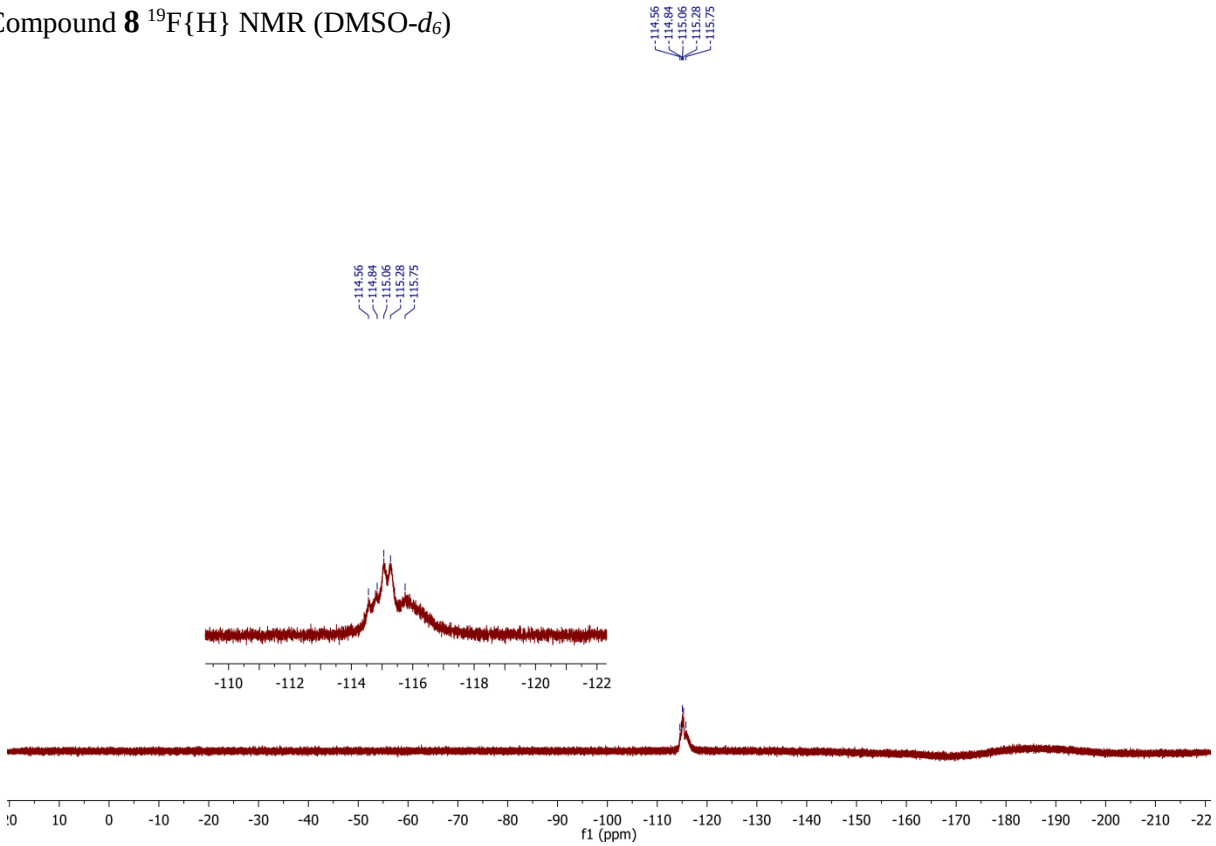
$C_{19}H_{17}F_2N_2O_8P$



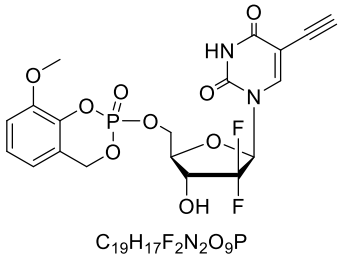
Compound **8** $^{31}P\{H\}$ NMR (DMSO-d_6)



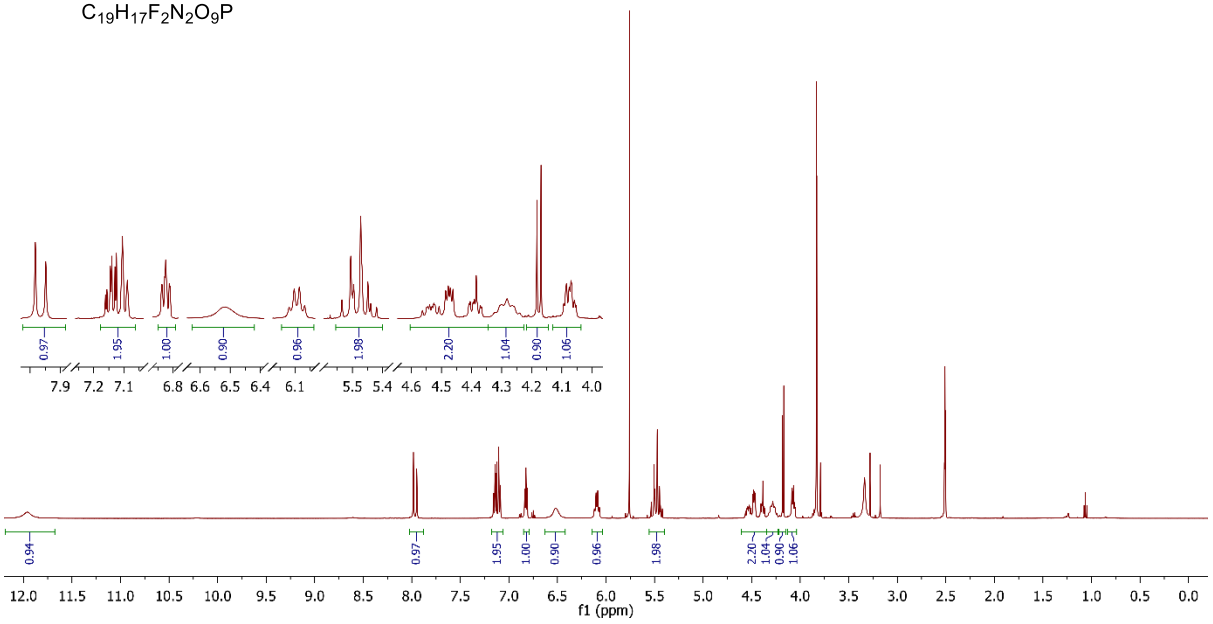
Compound **8** $^{19}F\{H\}$ NMR (DMSO-d_6)

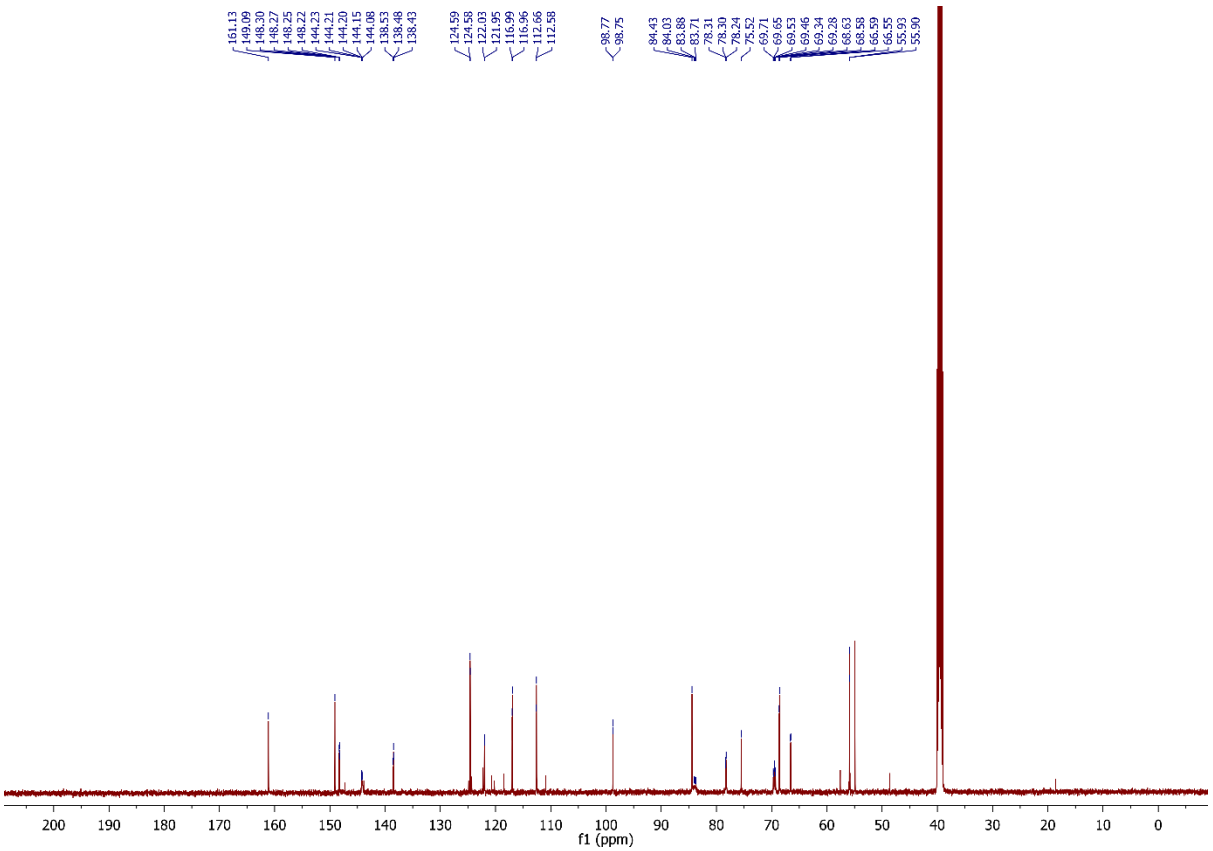


Compound **9** ^{1}H and ^{13}C NMR (DMSO-d_6)

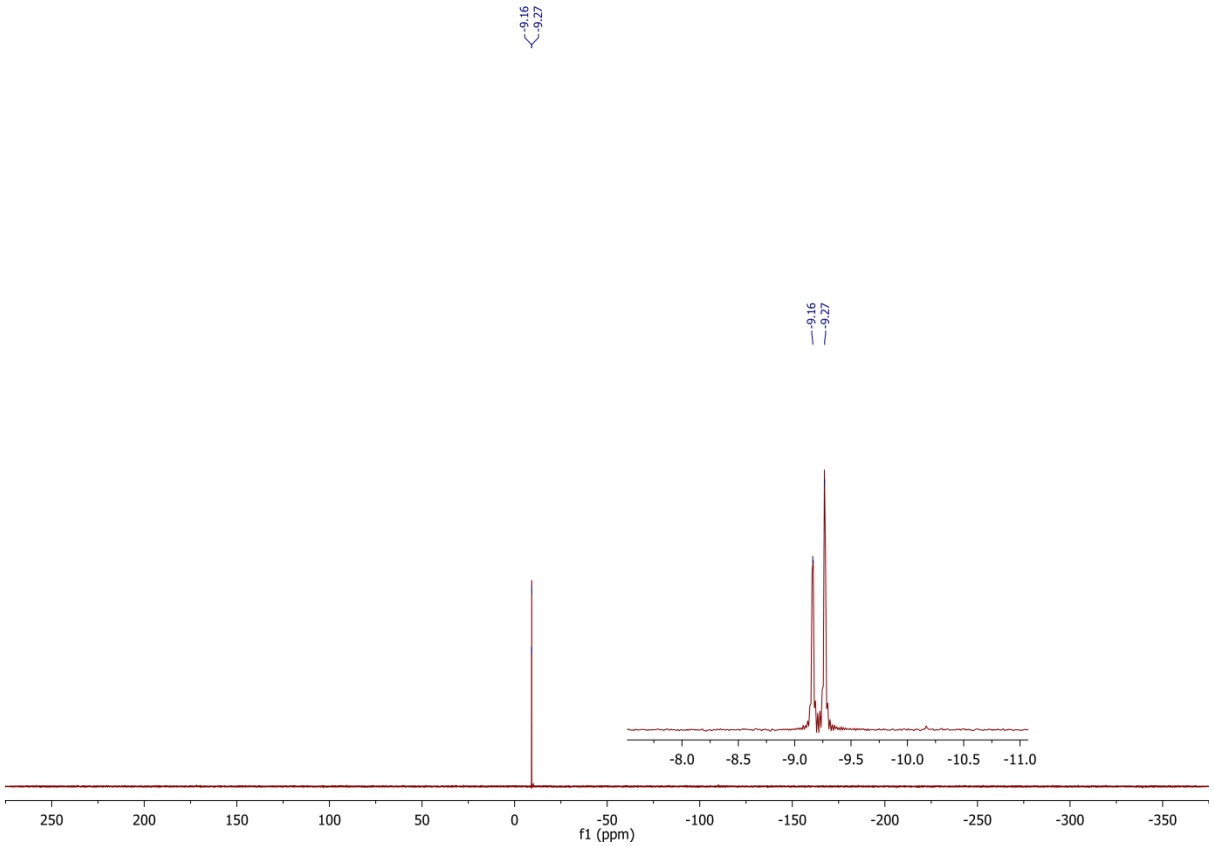


$C_{19}H_{17}F_2N_2O_9P$

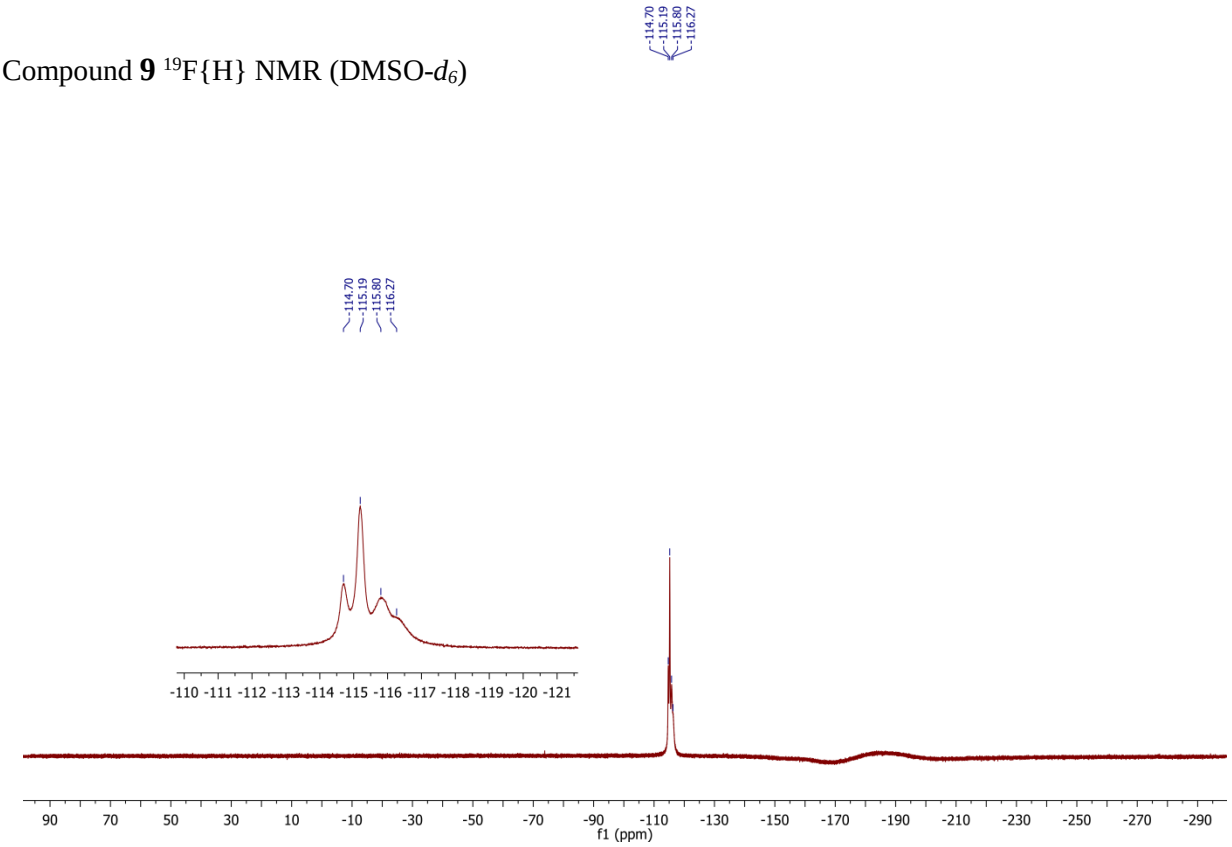




Compound **9** $^{31}P\{H\}$ NMR (DMSO-d_6)

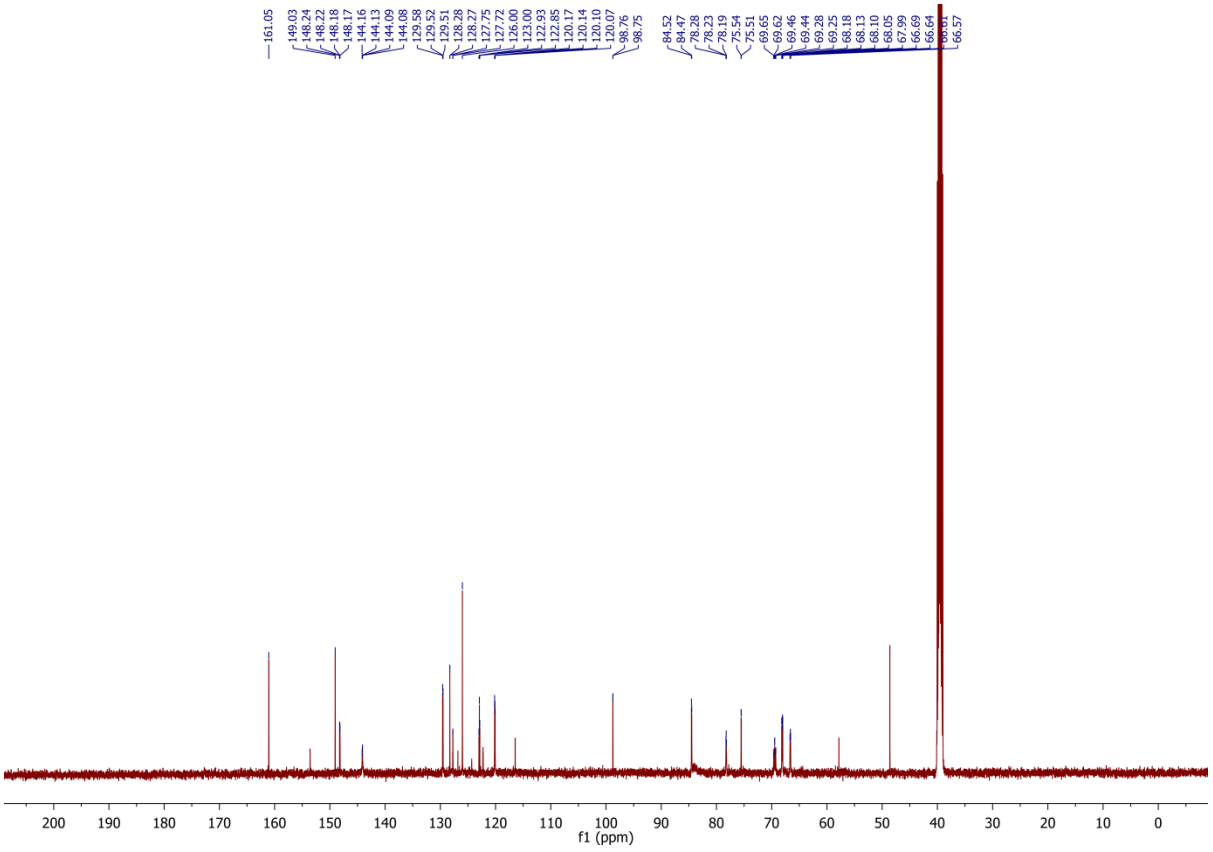


Compound **9** $^{19}F\{H\}$ NMR (DMSO-d_6)

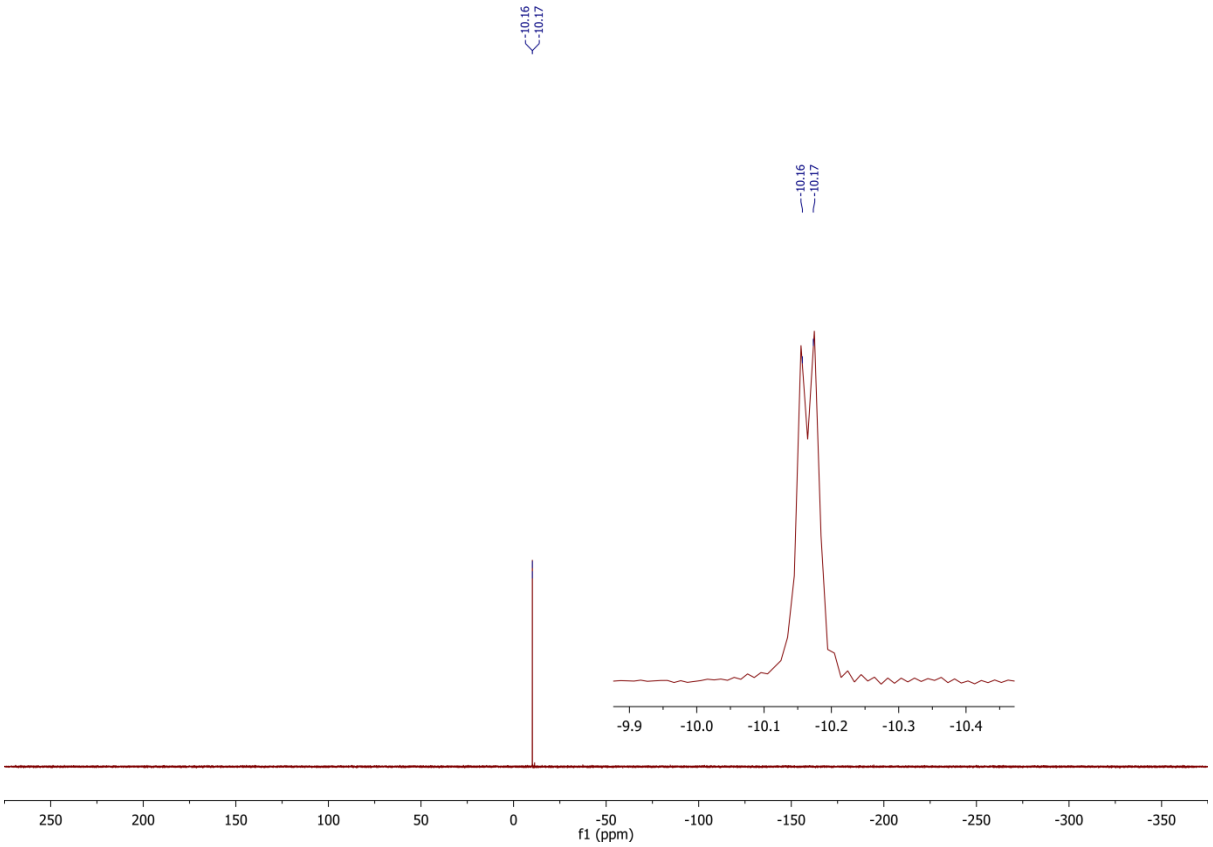


Compound **10** ^{1}H and ^{13}C NMR (DMSO-d_6)

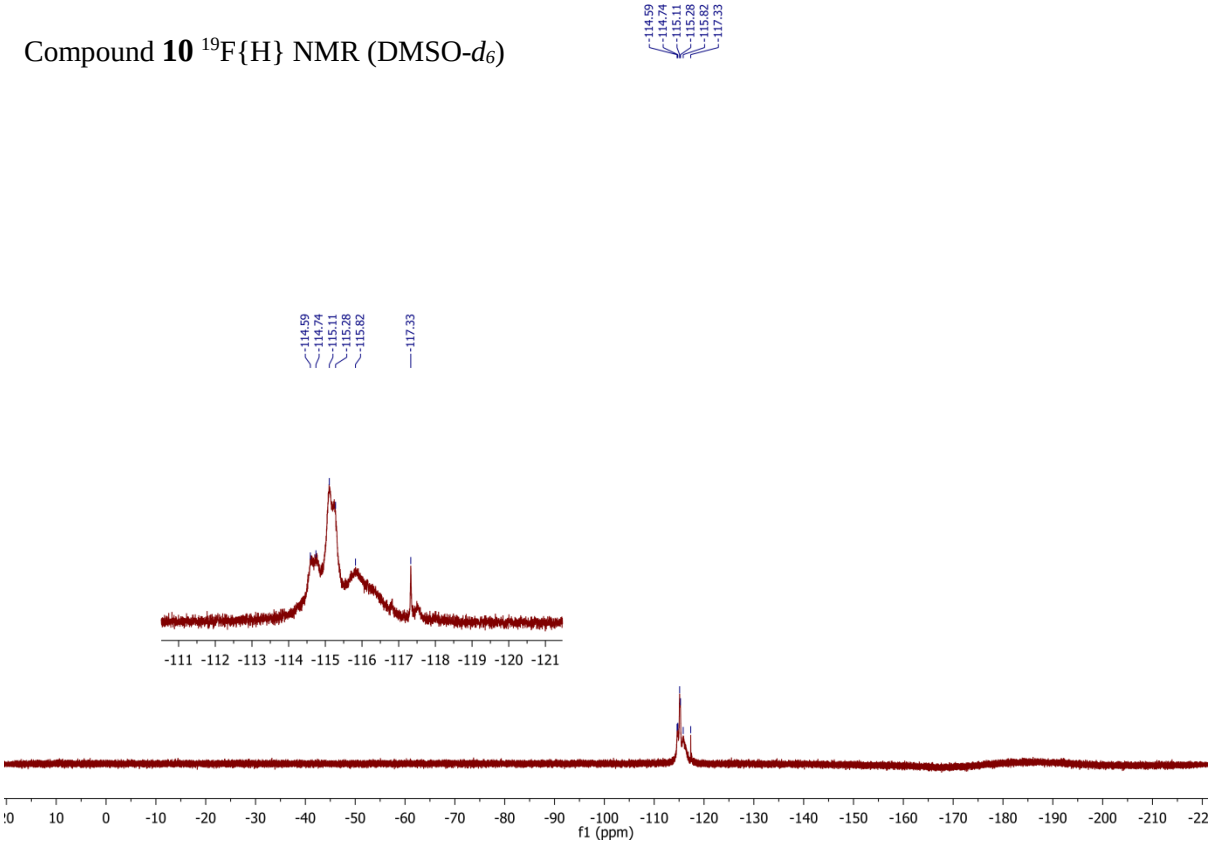
$C_{18}H_{14}ClF_2N_2O_8P$



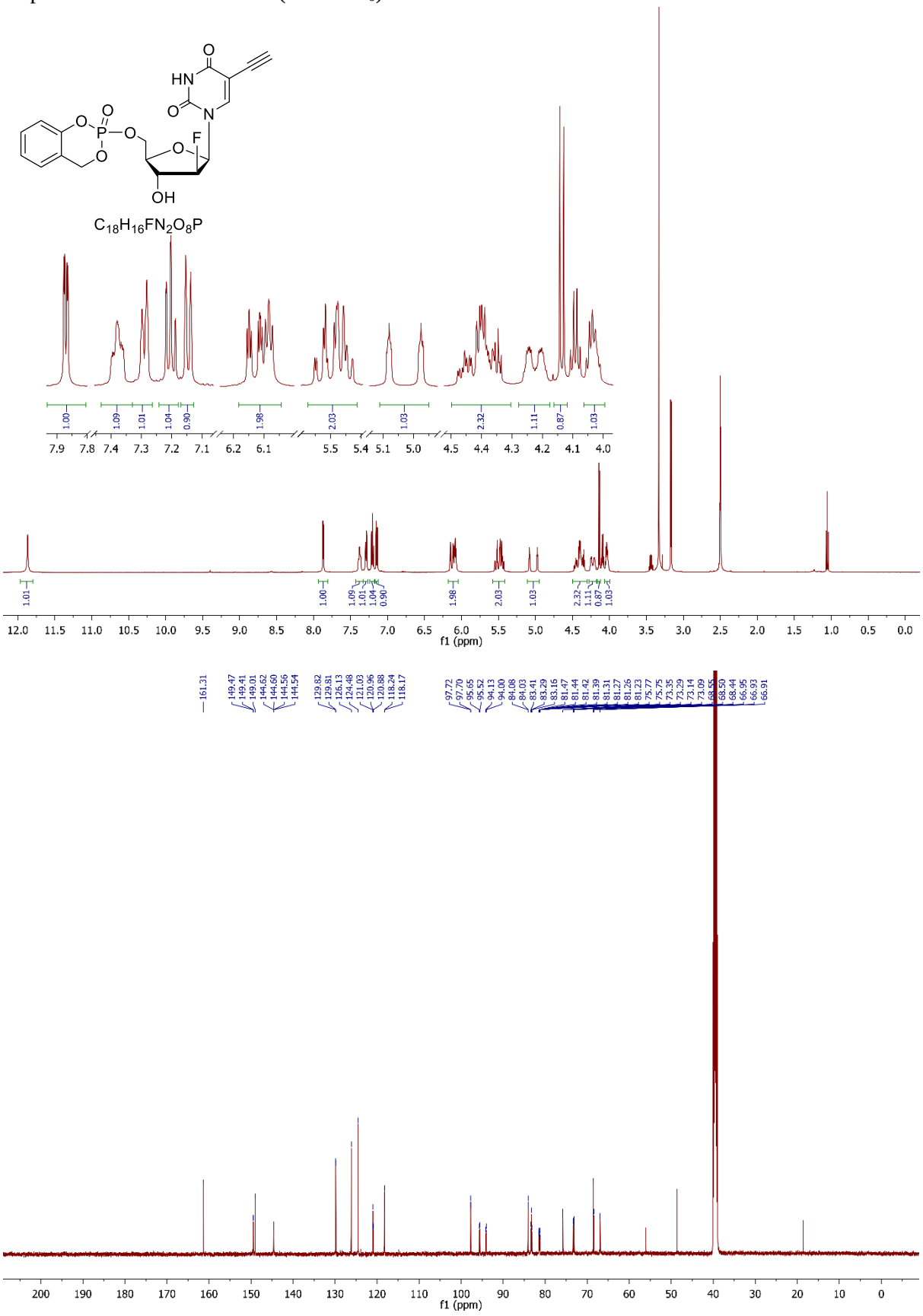
Compound **10** $^{31}P\{H\}$ NMR (DMSO-d_6)



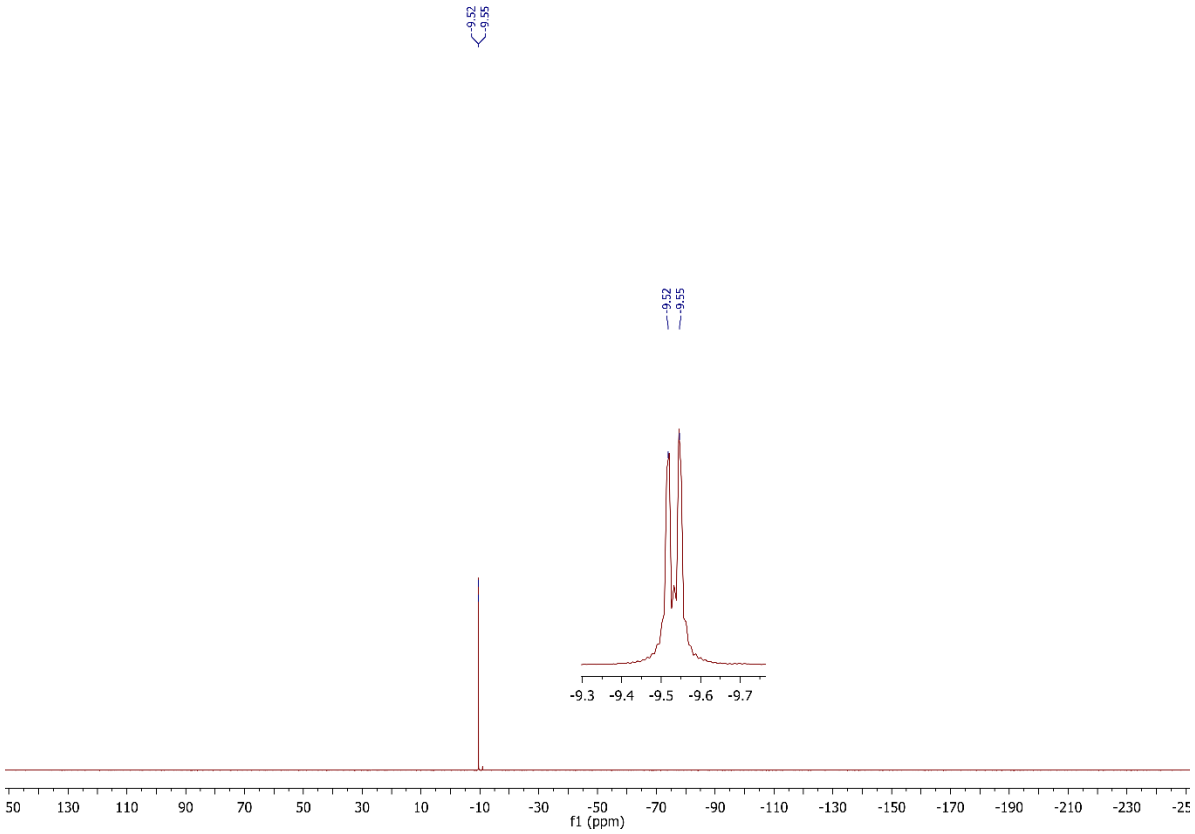
Compound **10** $^{19}F\{H\}$ NMR (DMSO-d_6)



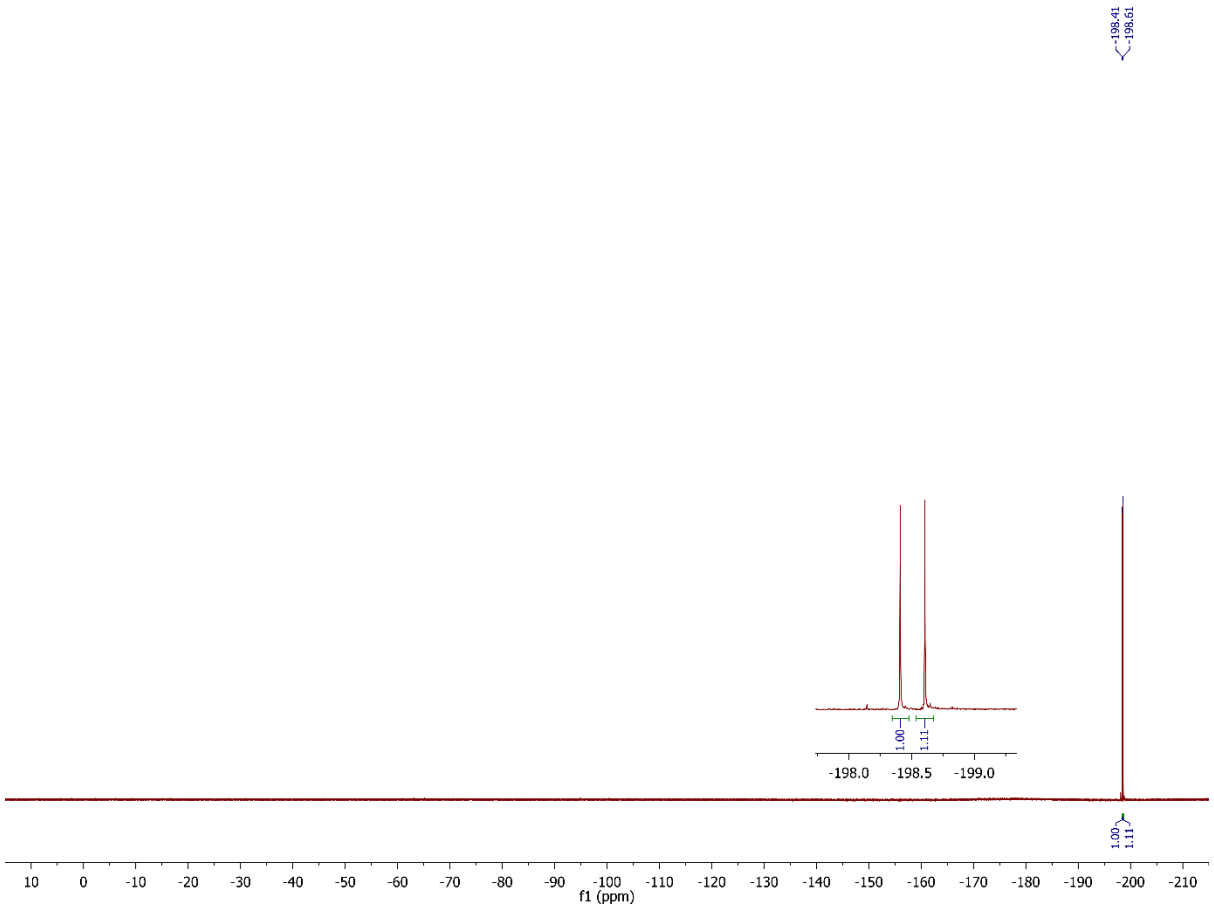
Compound **11** ^{1}H and ^{13}C NMR (DMSO-d_6)



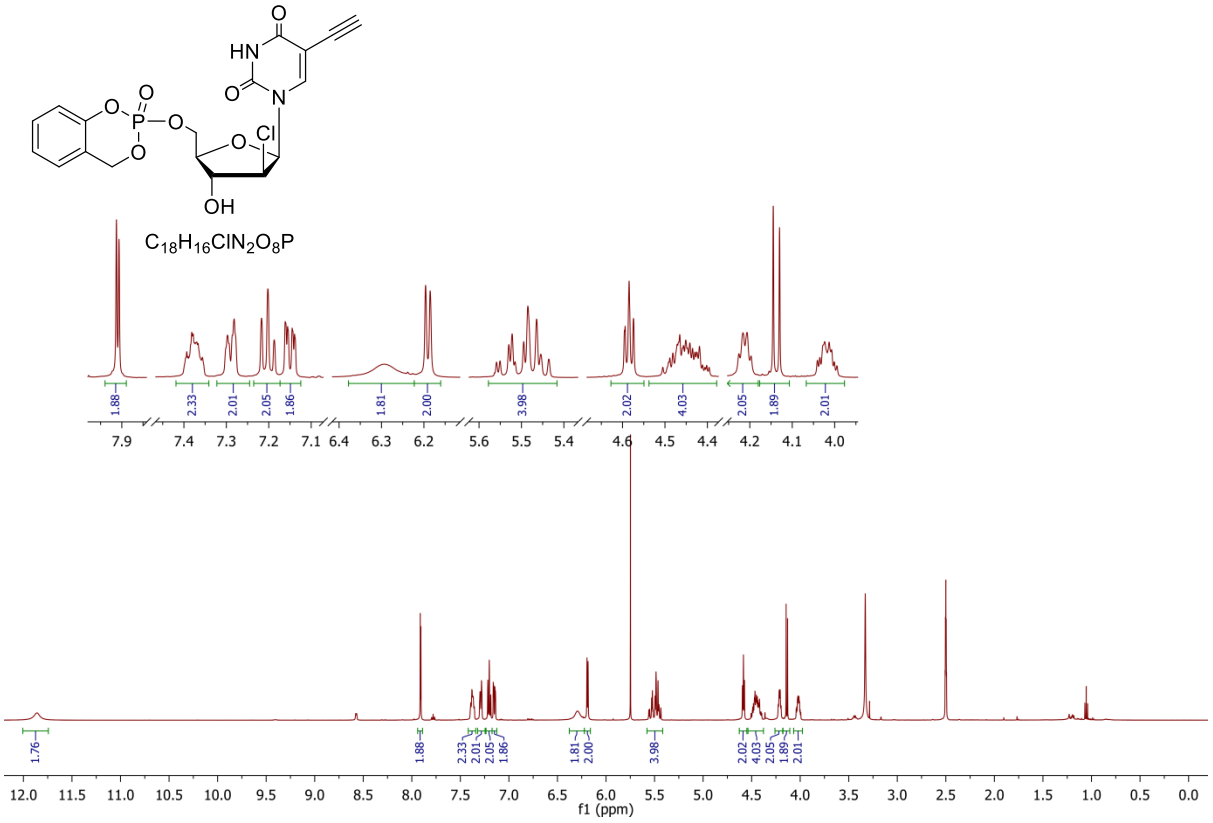
Compound **11** $^{31}P\{H\}$ NMR (DMSO-d_6)

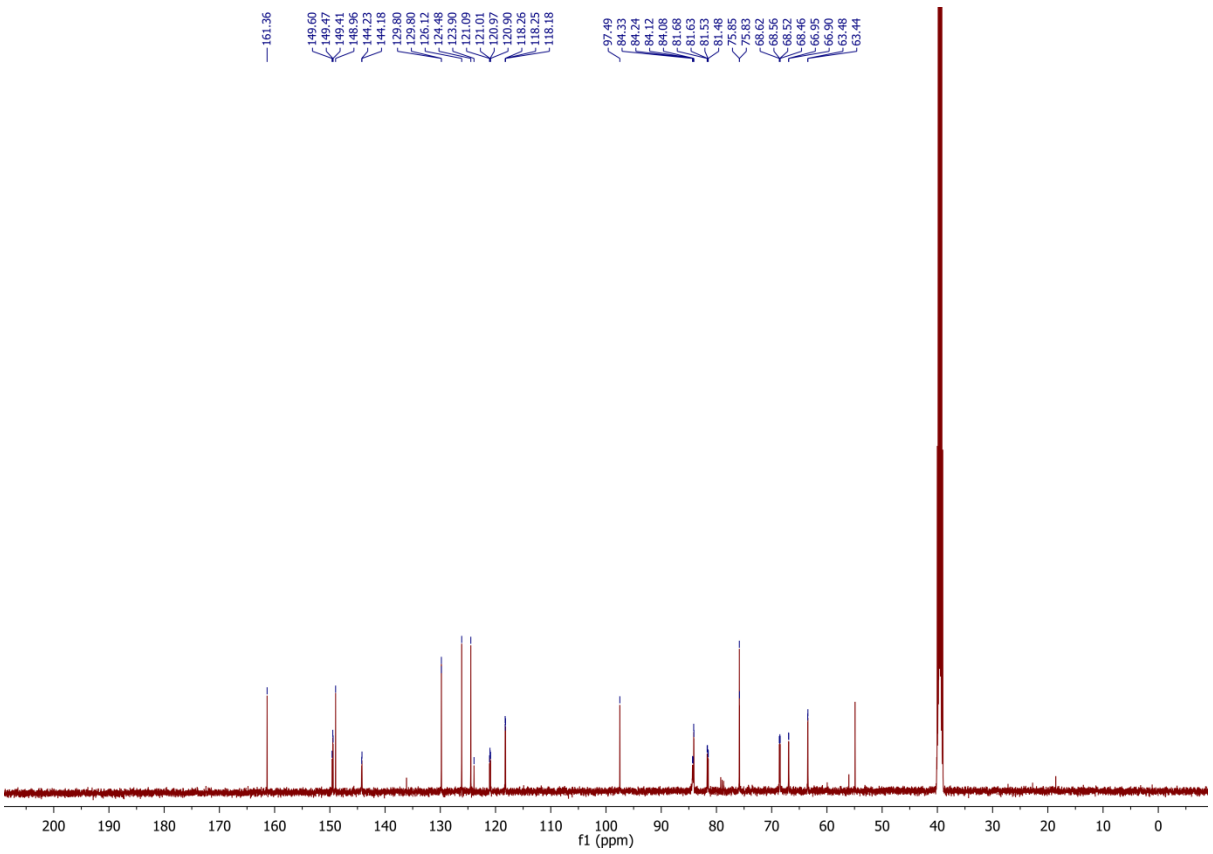


Compound **11** $^{19}F\{H\}$ NMR (DMSO-d_6)

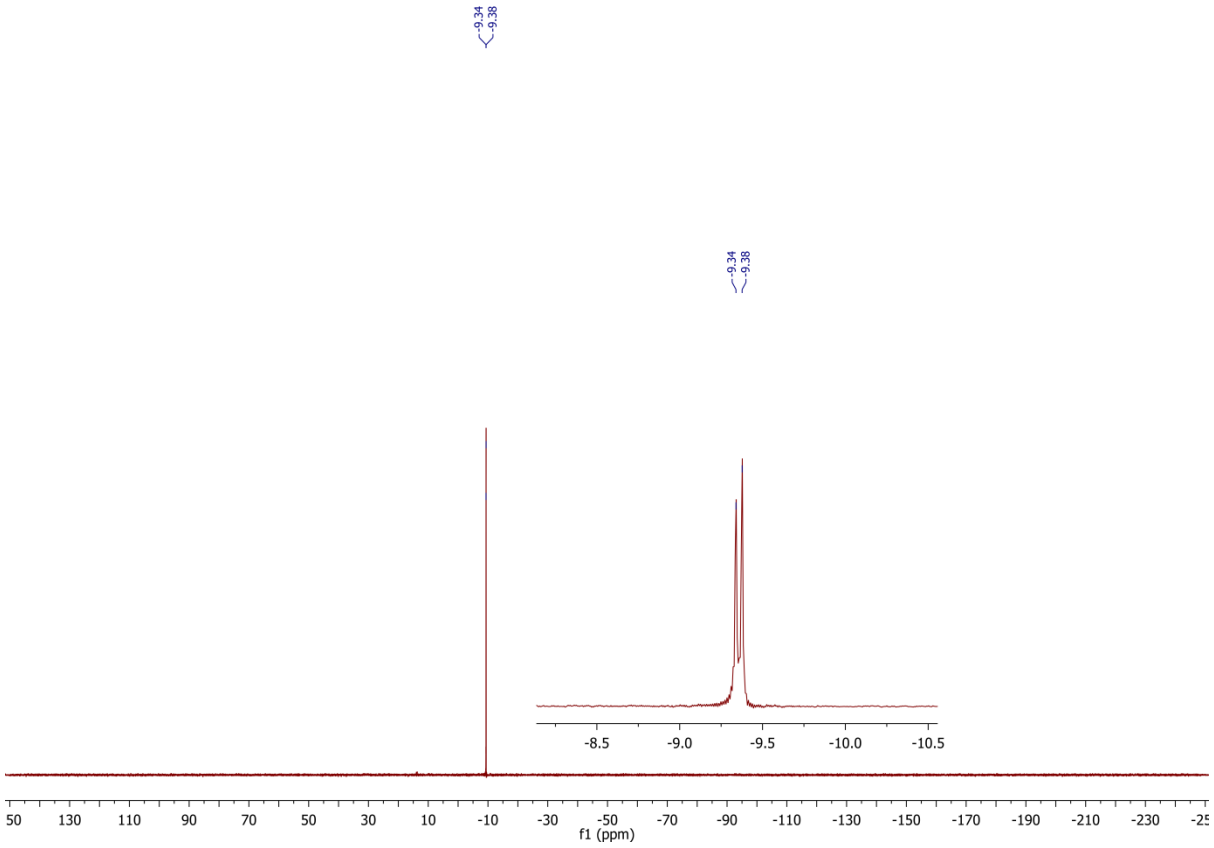


Compound **12** ^{1}H and ^{13}C NMR (DMSO-d_6)

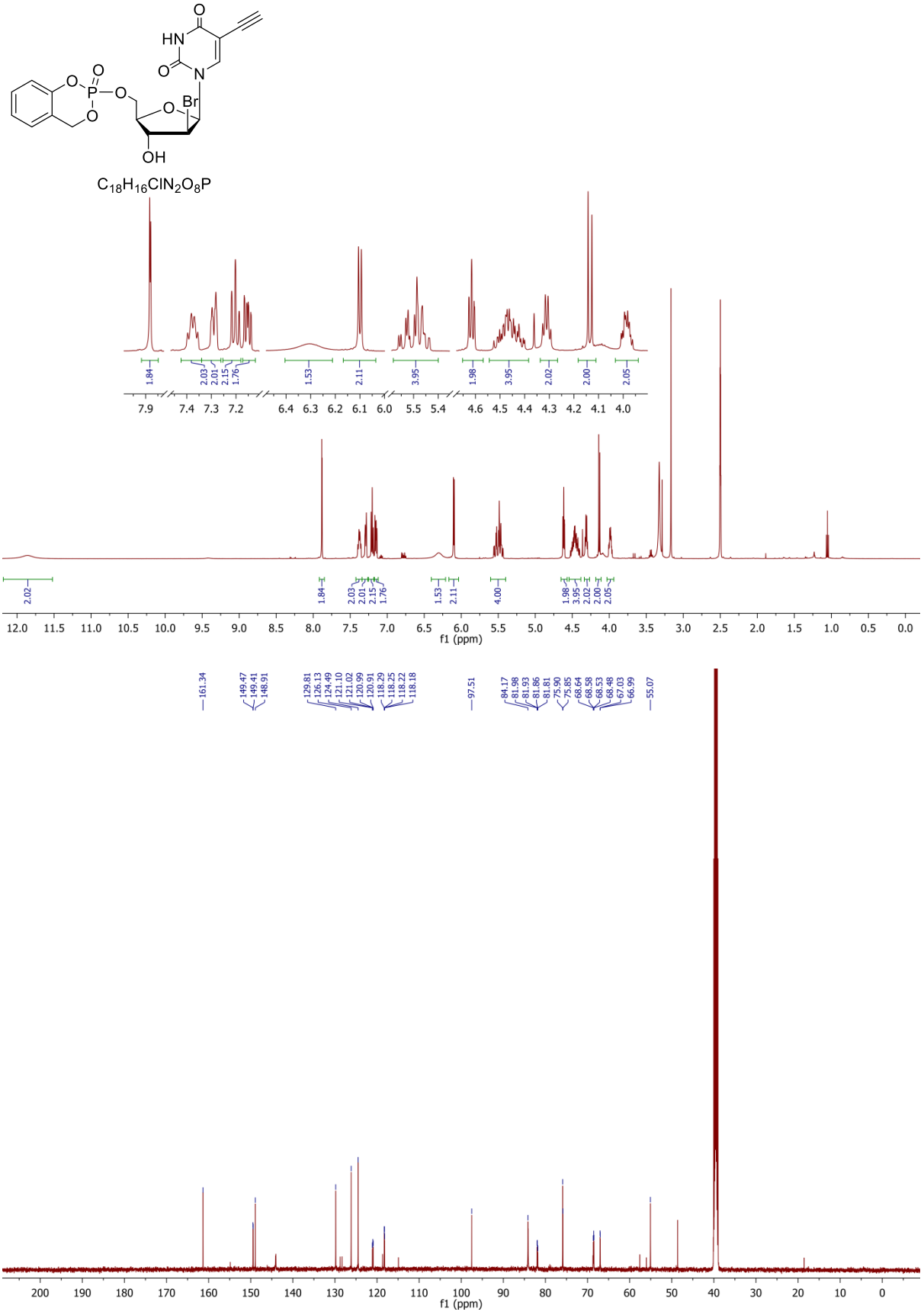




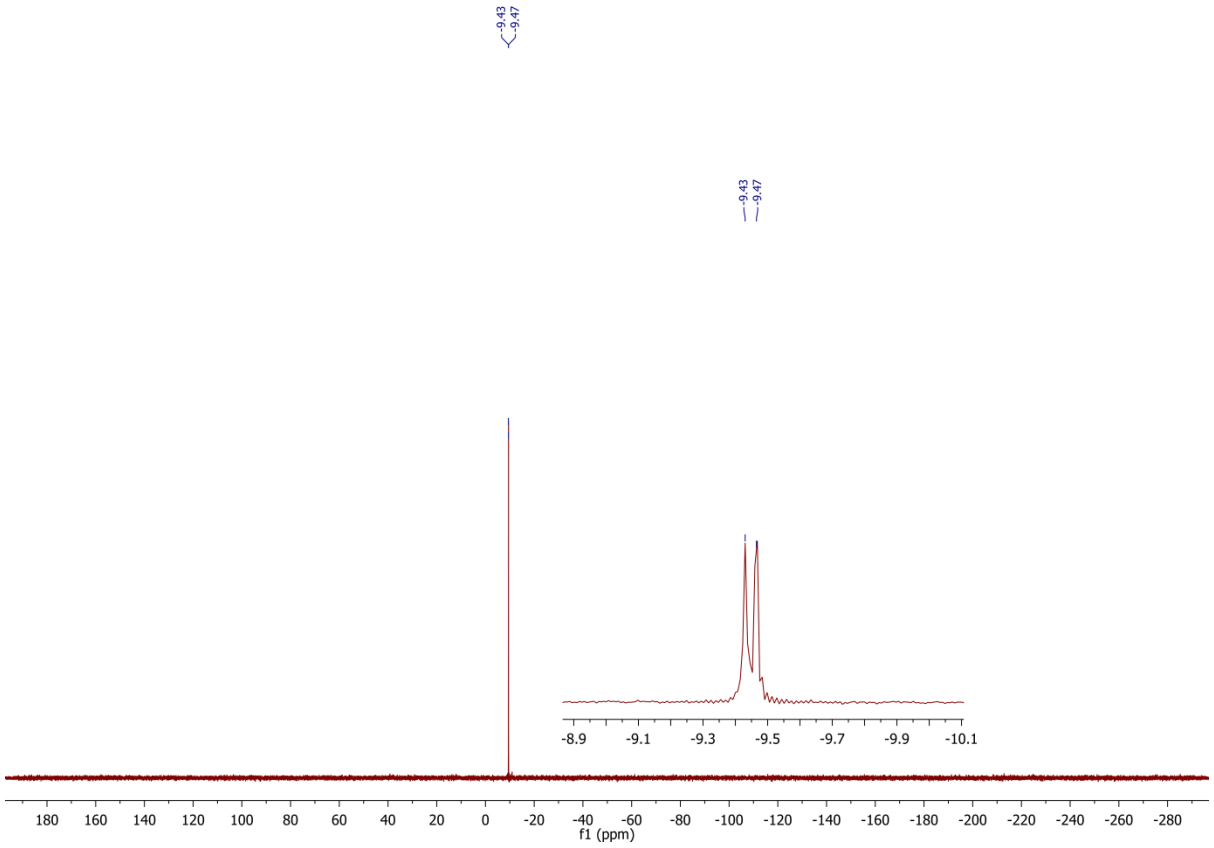
Compound **12** $^{31}P\{H\}$ NMR (DMSO-d_6)



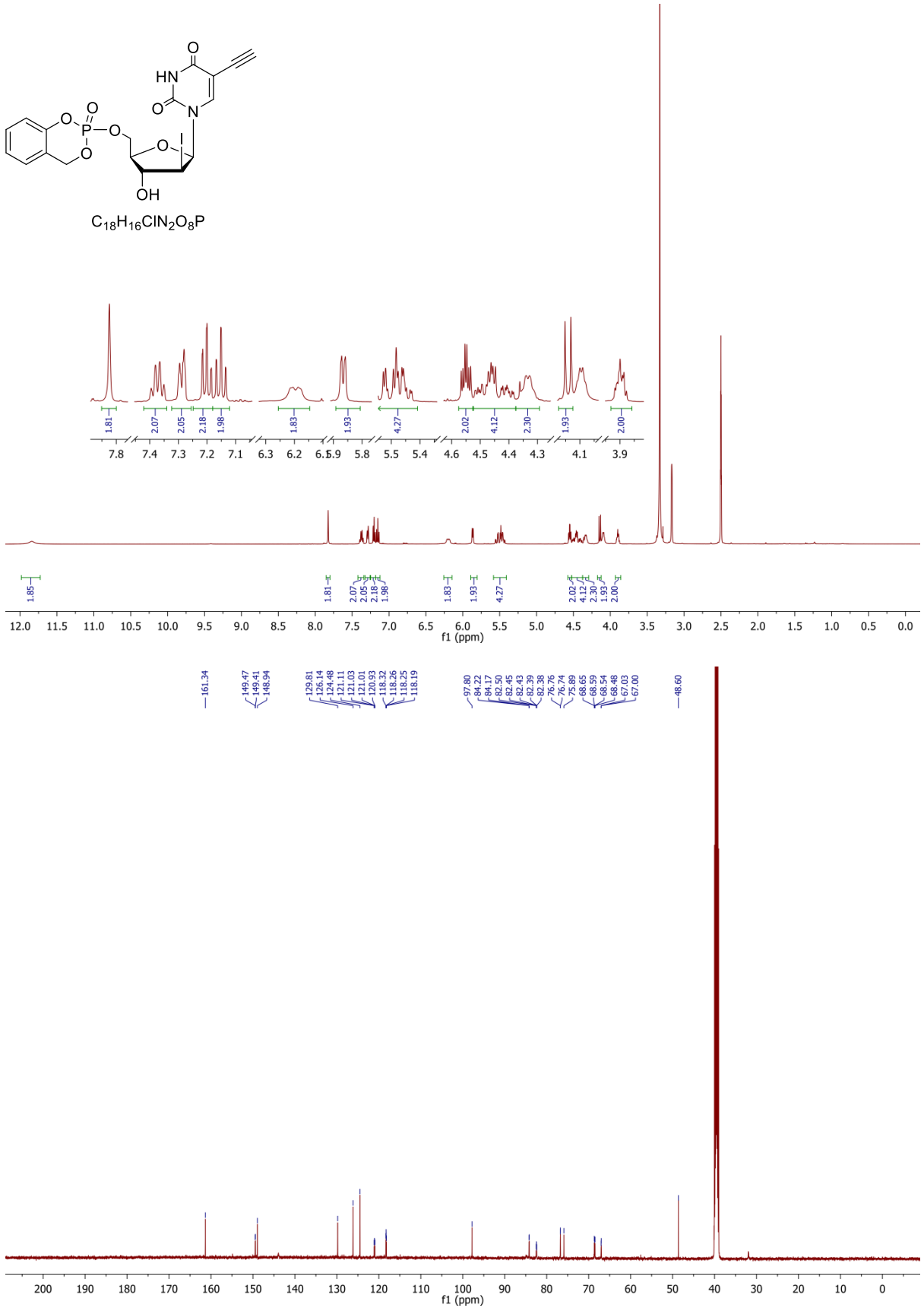
Compound **13** ^{1}H and ^{13}C NMR (DMSO-d_6)



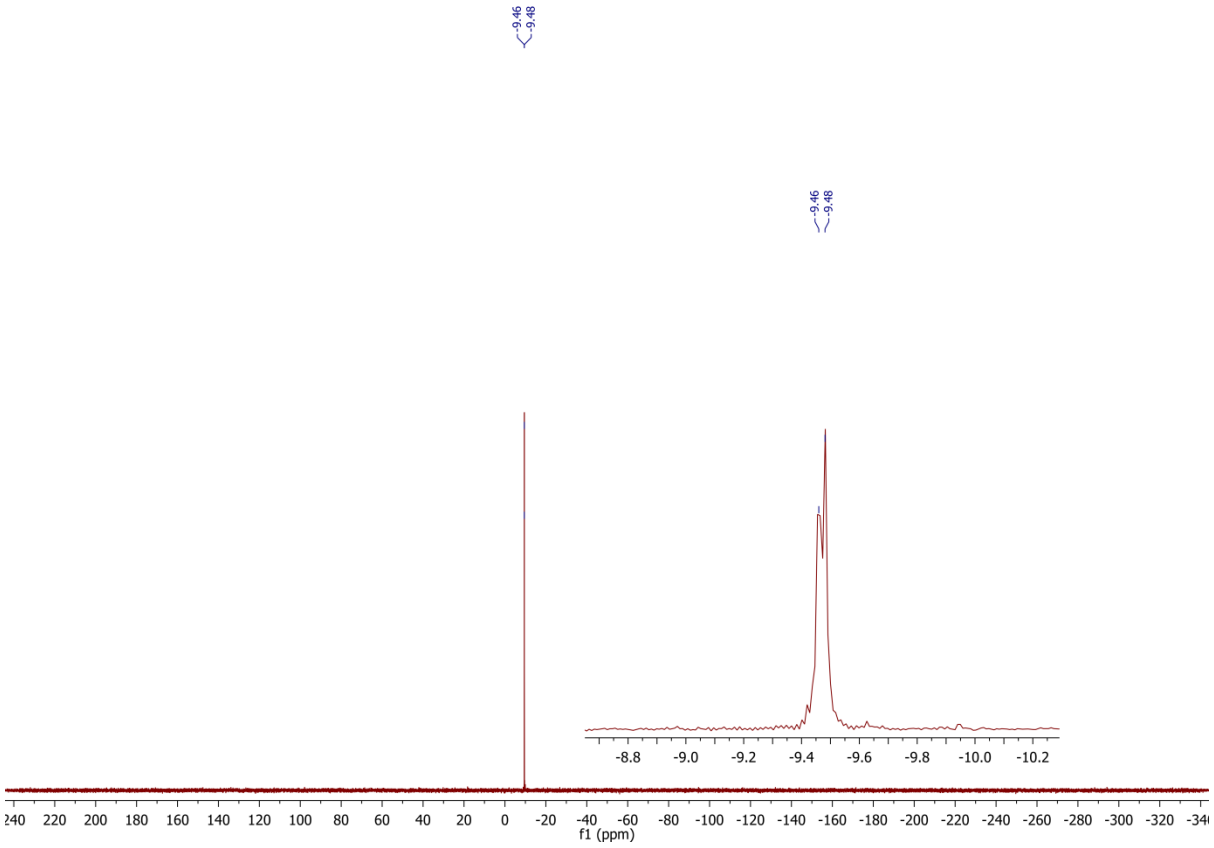
Compound **13** $^{31}P\{H\}$ NMR (DMSO-d_6)



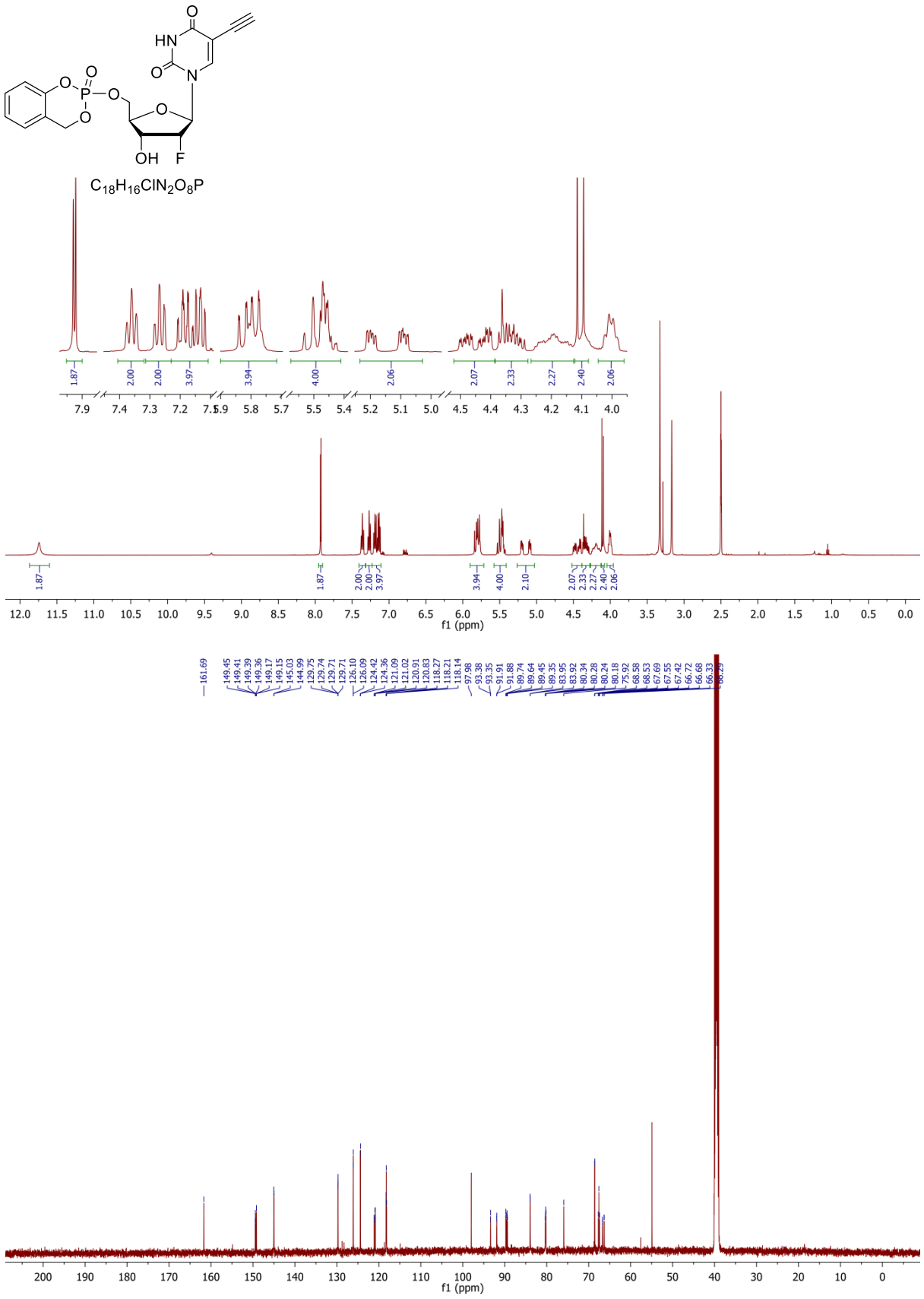
Compound **14** ^{1}H and ^{13}C NMR (DMSO-d_6)



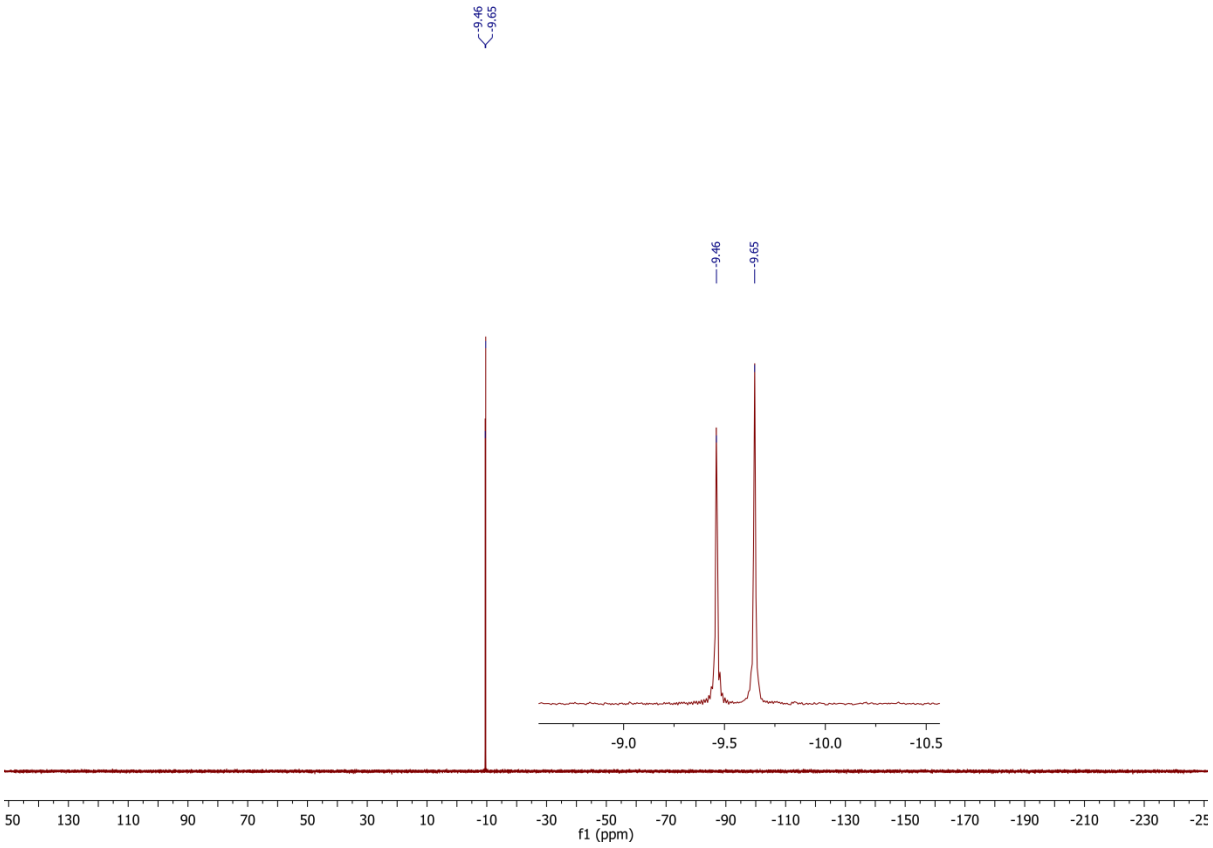
Compound **14** $^{31}P\{H\}$ NMR (DMSO-d_6)



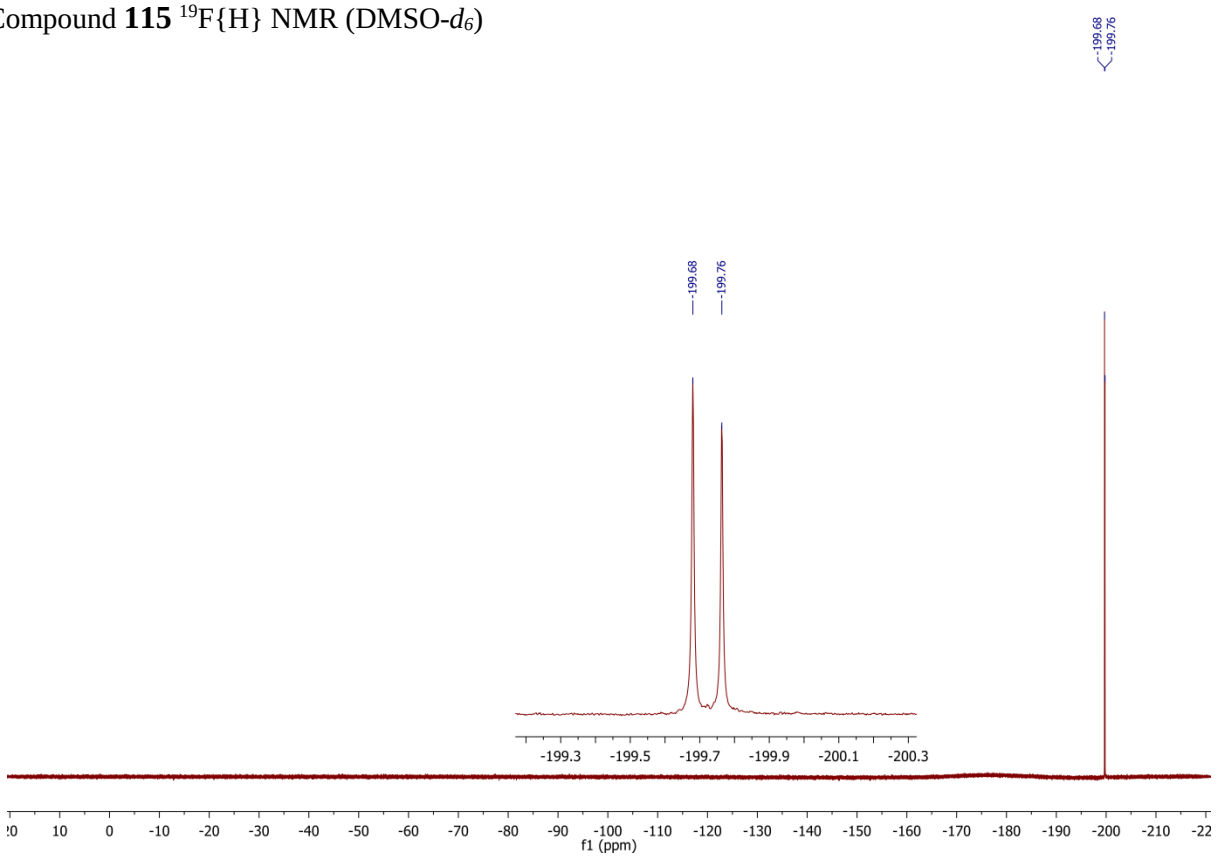
Compound **15** ^{1}H and ^{13}C NMR (DMSO-d_6)



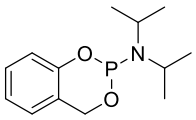
Compound **15** $^{31}P\{H\}$ NMR (DMSO-d_6)



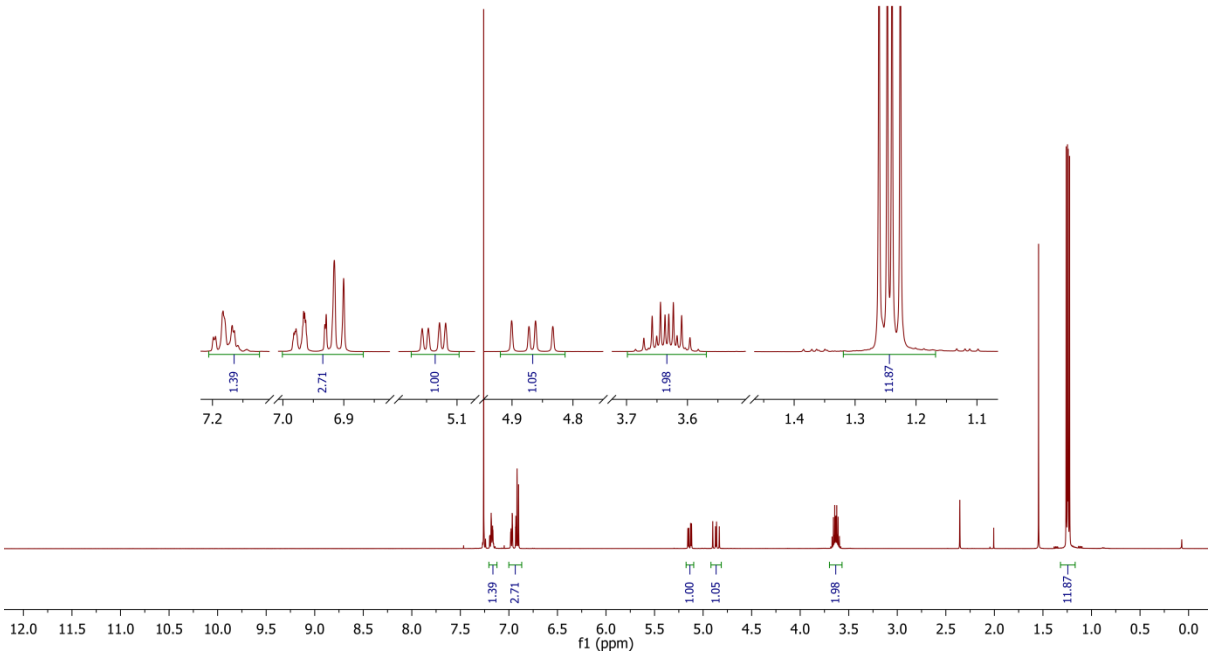
Compound **115** $^{19}F\{H\}$ NMR (DMSO-d_6)

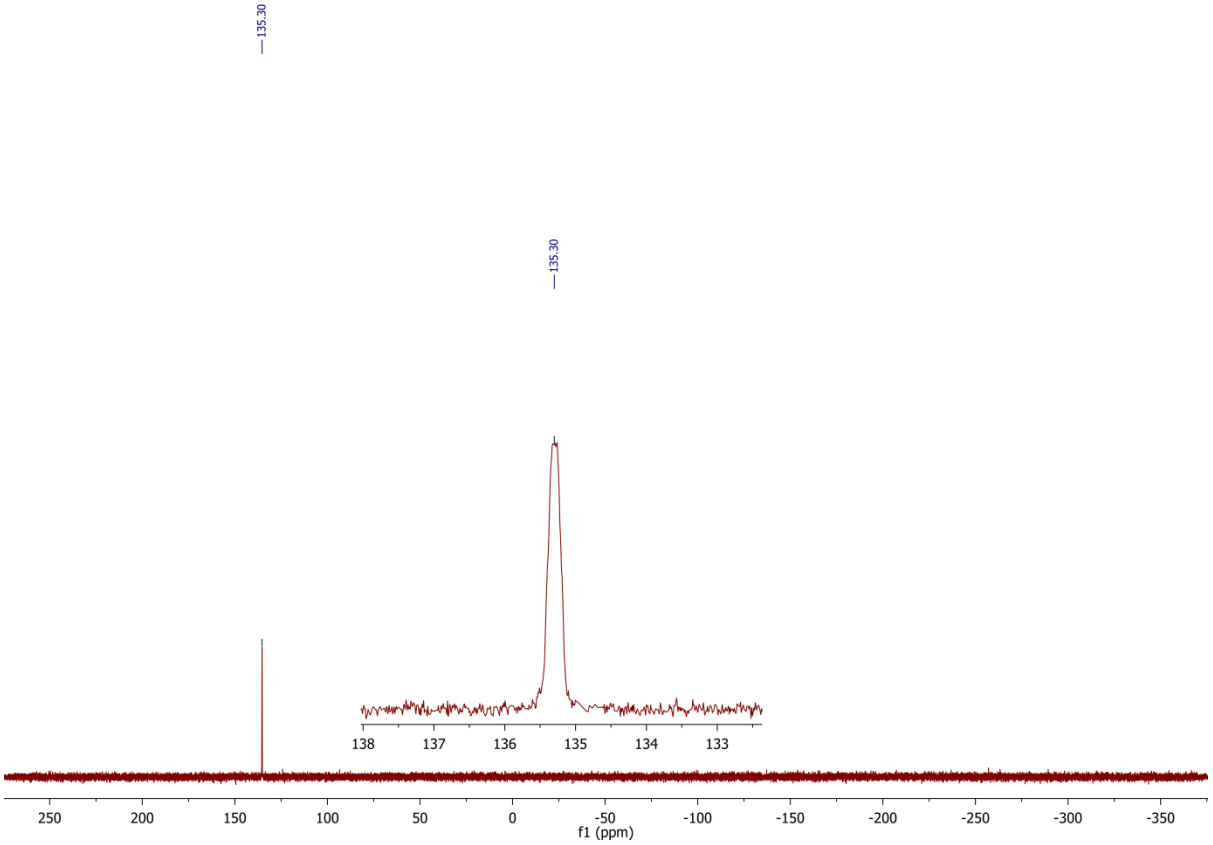


Compound **20** ^{1}H and ^{31}P NMR (CDCl3)

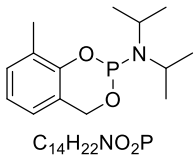


$C_{13}H_{20}NO_2P$

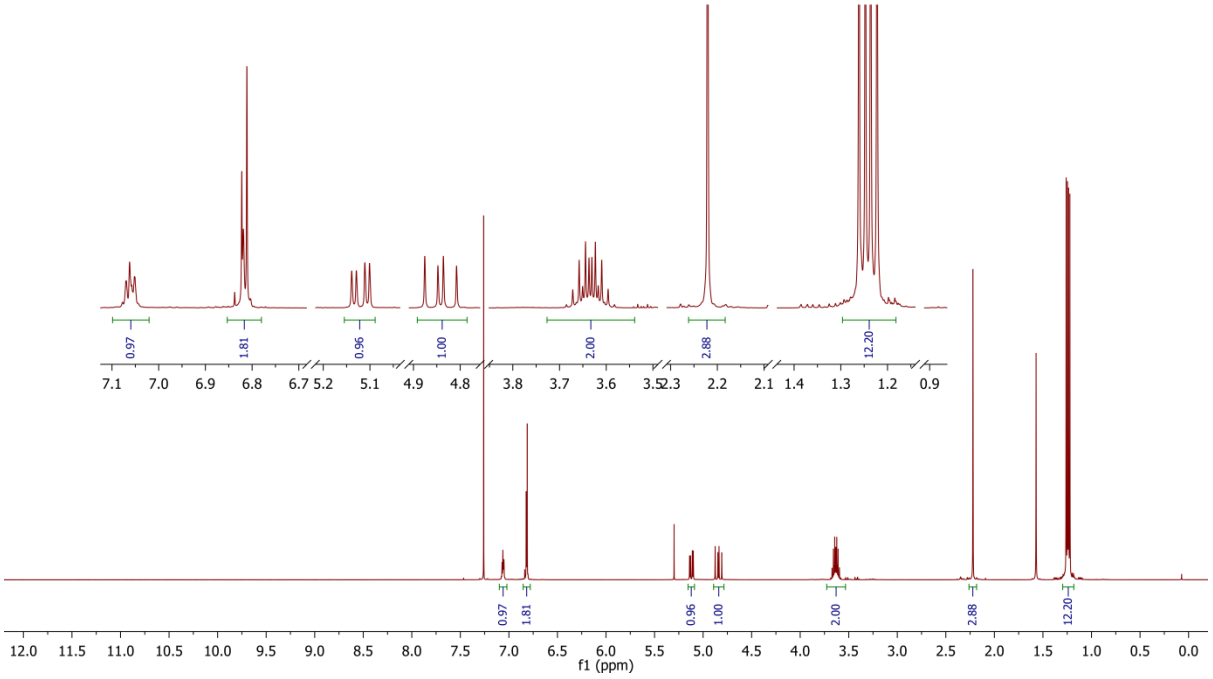


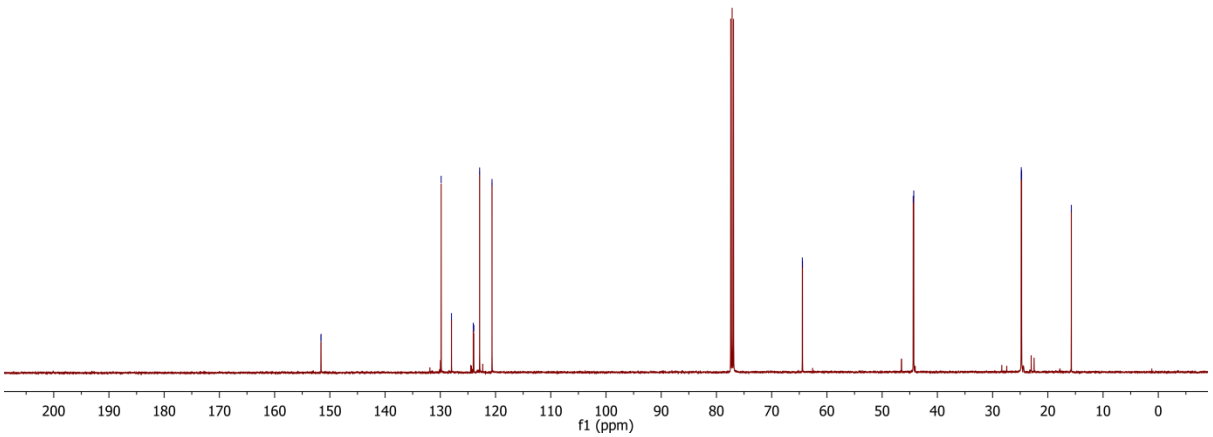


Compound **24** ^{1}H and ^{13}C NMR ($CDCl_3$)

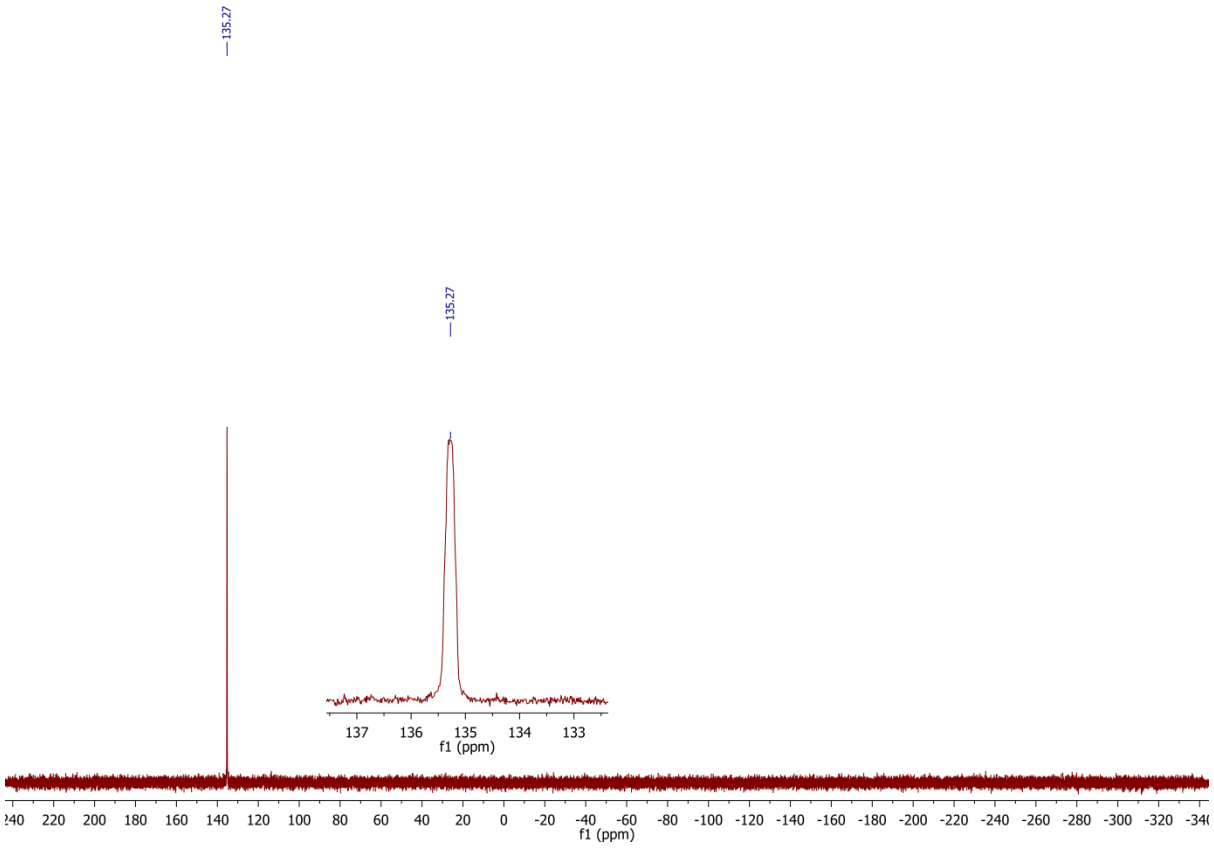


$C_{14}H_{22}NO_2P$

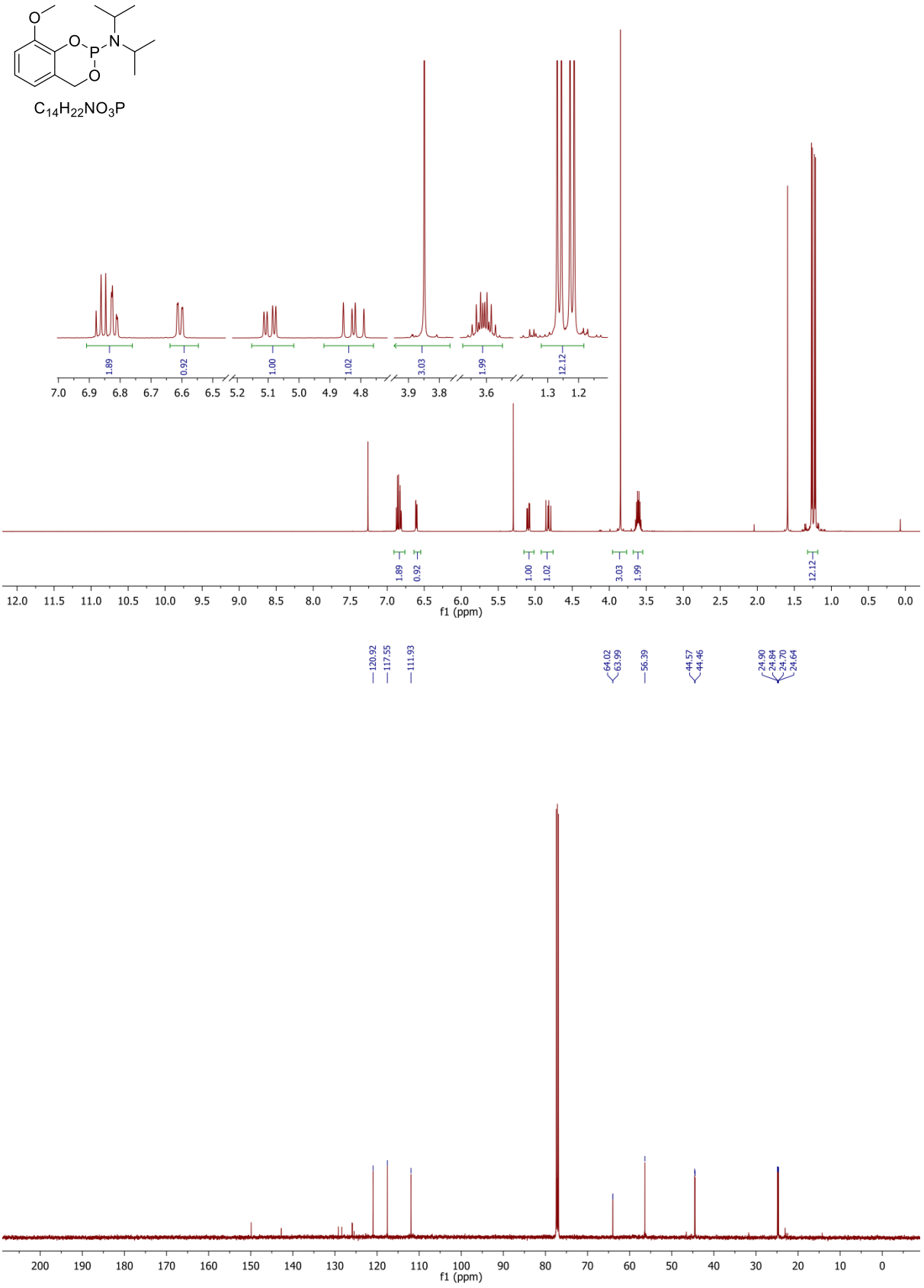




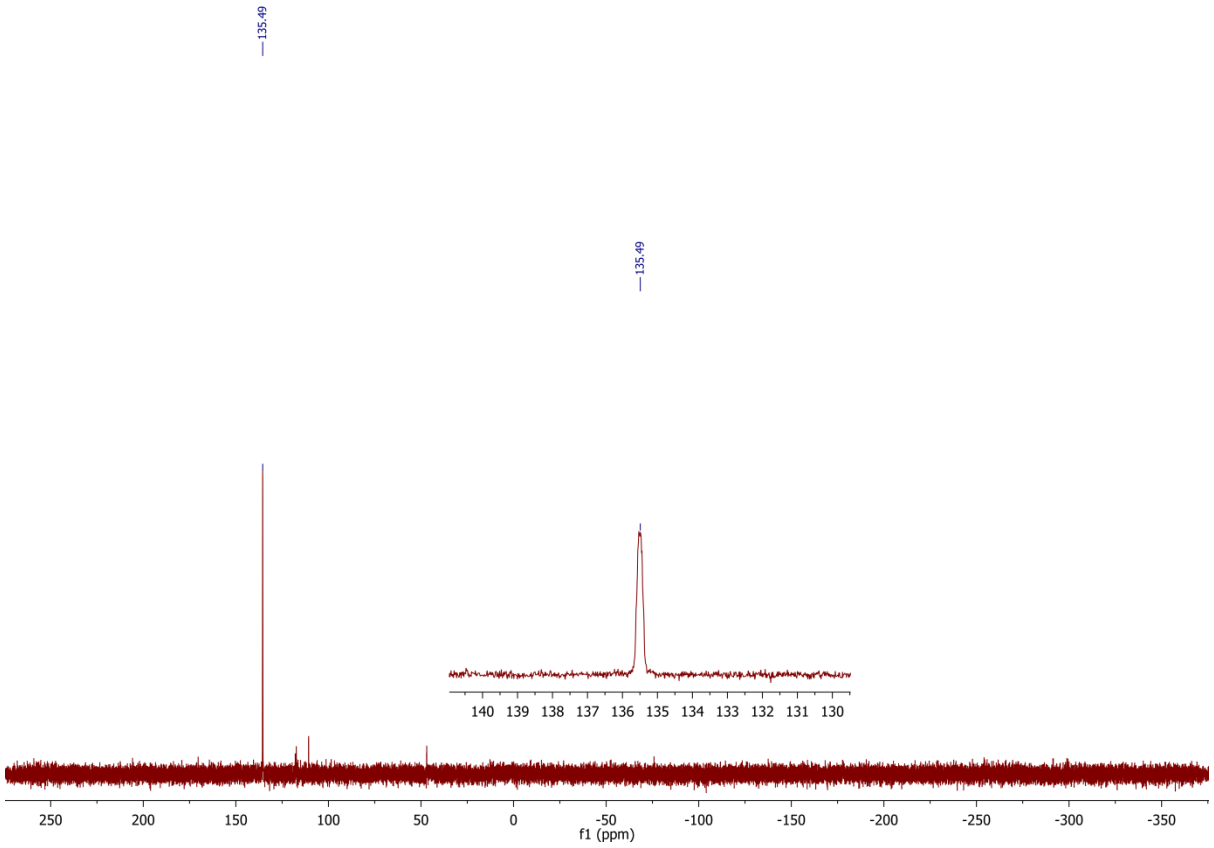
Compound **24** ^{31}P NMR ($CDCl_3$)



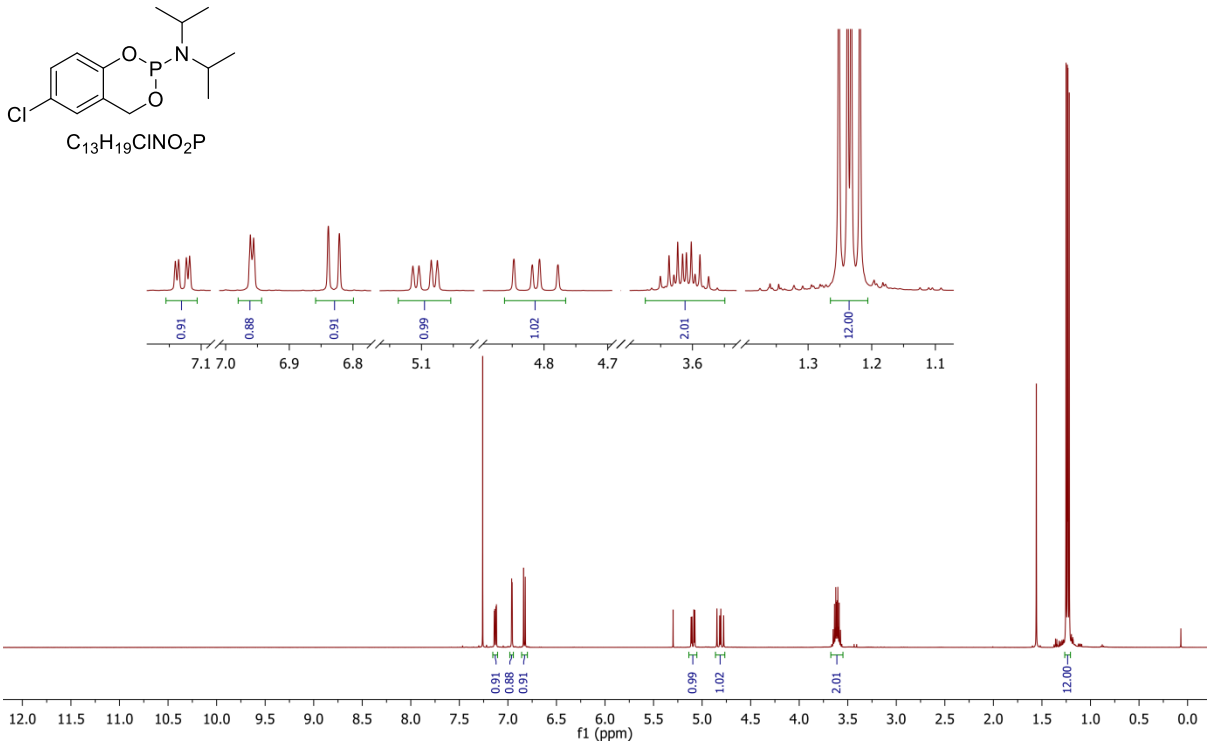
Compound **25** ^{1}H and ^{13}C NMR ($CDCl_3$)

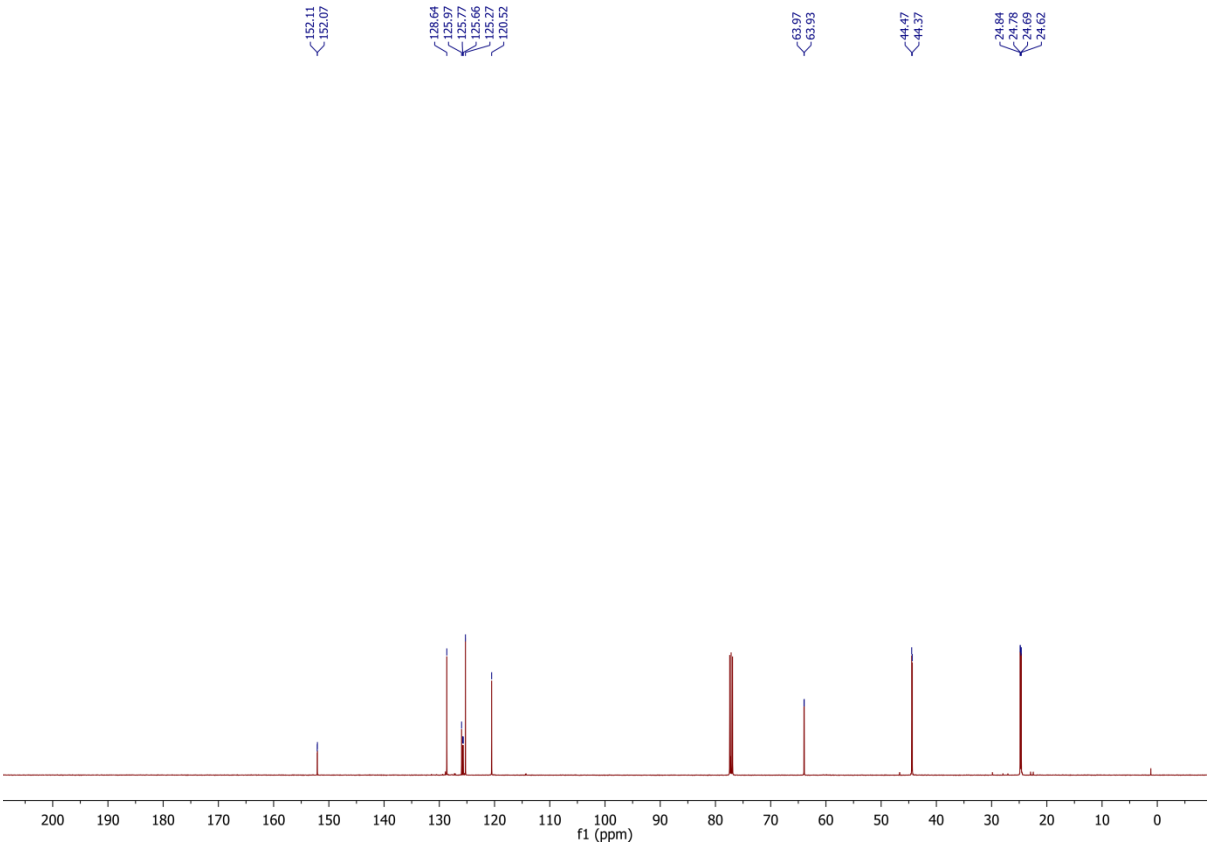


Compound **25** ^{31}P NMR ($CDCl_3$)

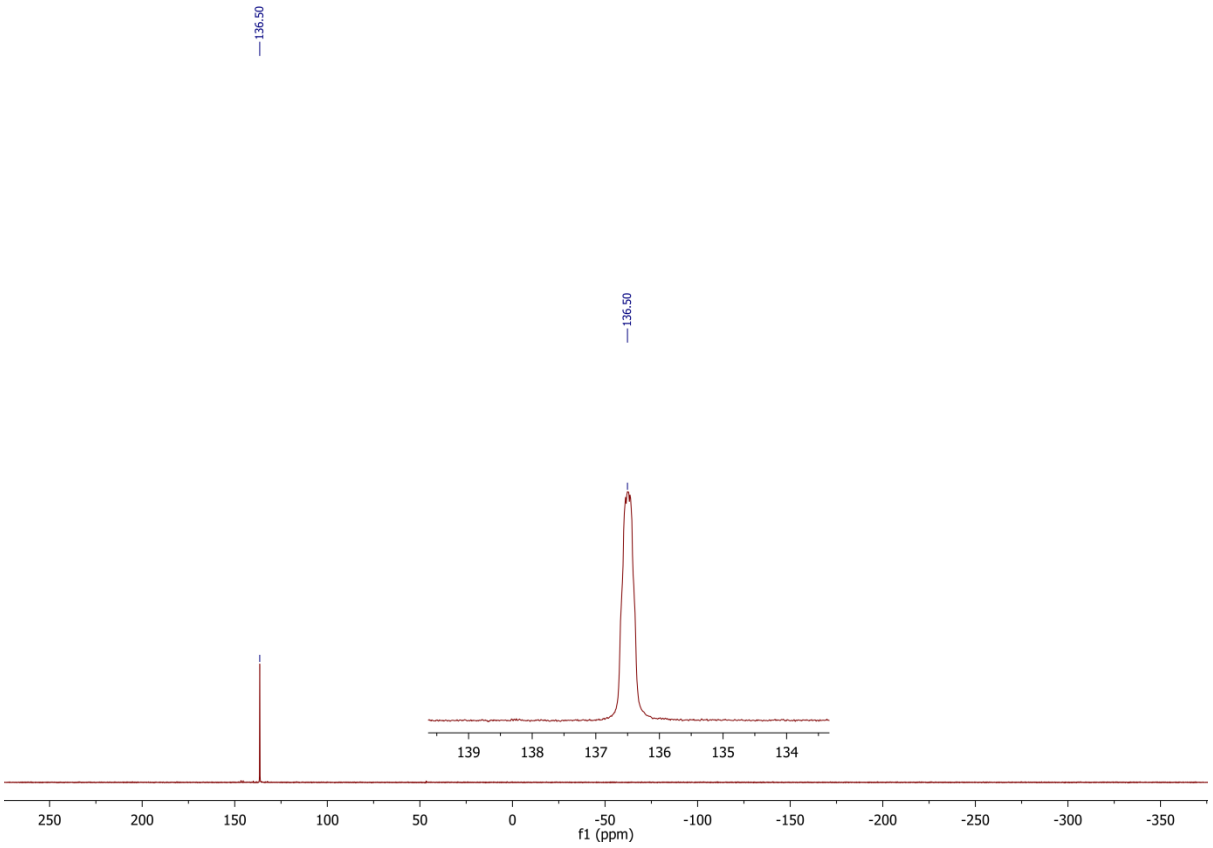


Compound **26** ^{1}H and ^{13}C NMR ($CDCl_3$)

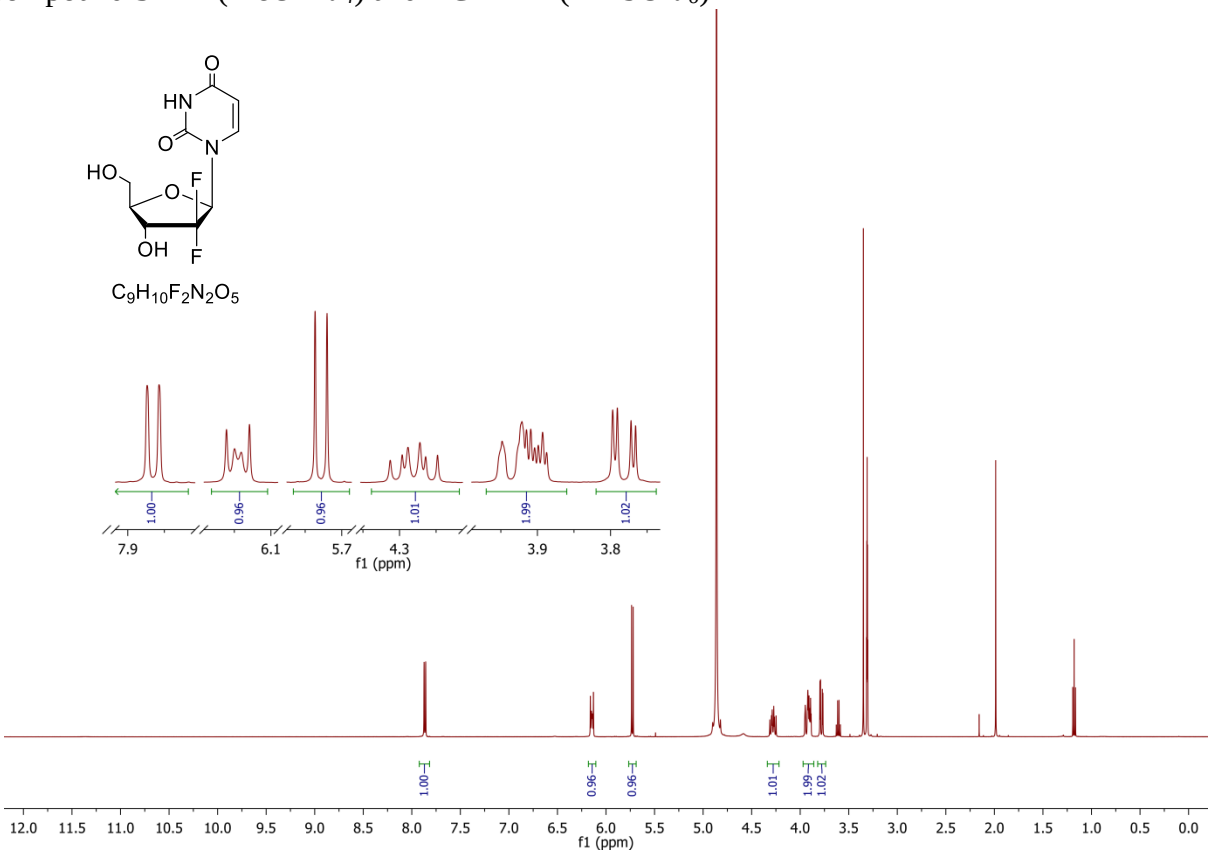


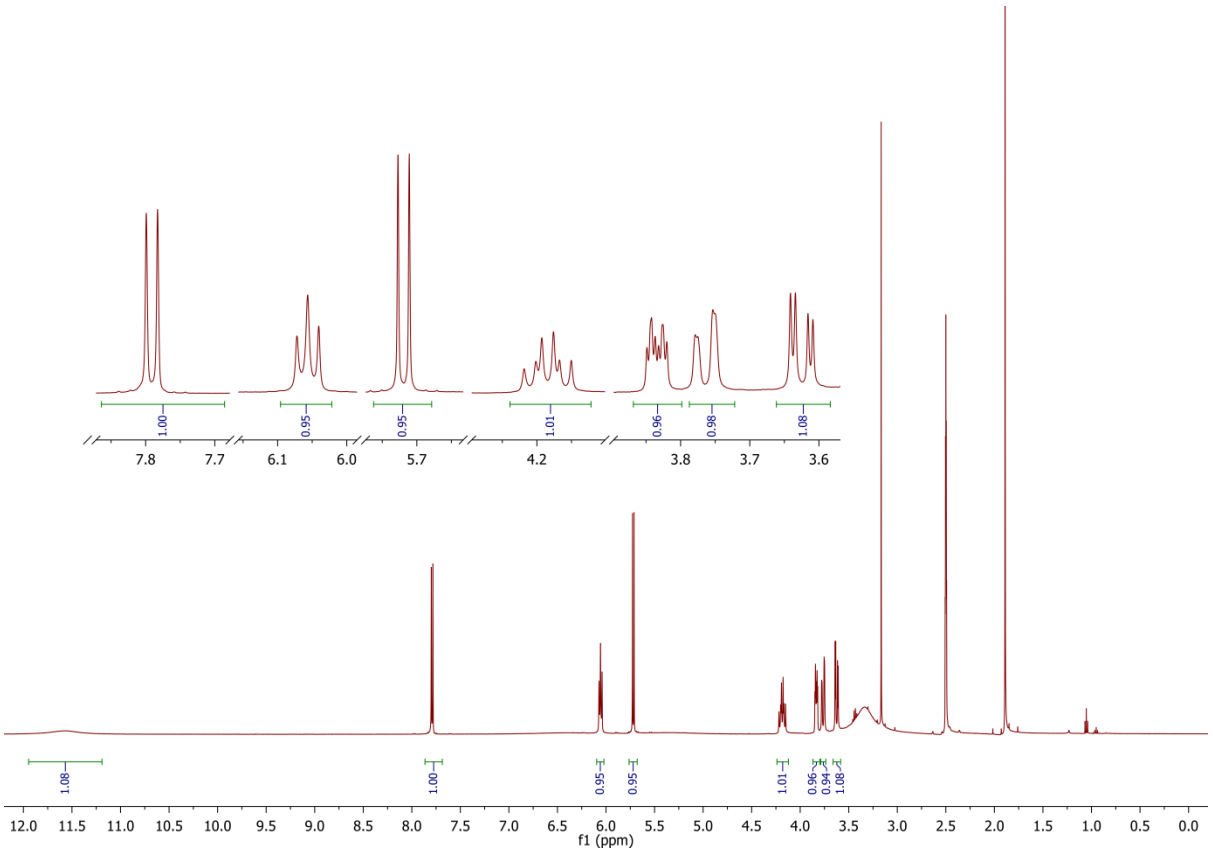


Compound **26** ^{31}P NMR ($CDCl_3$)

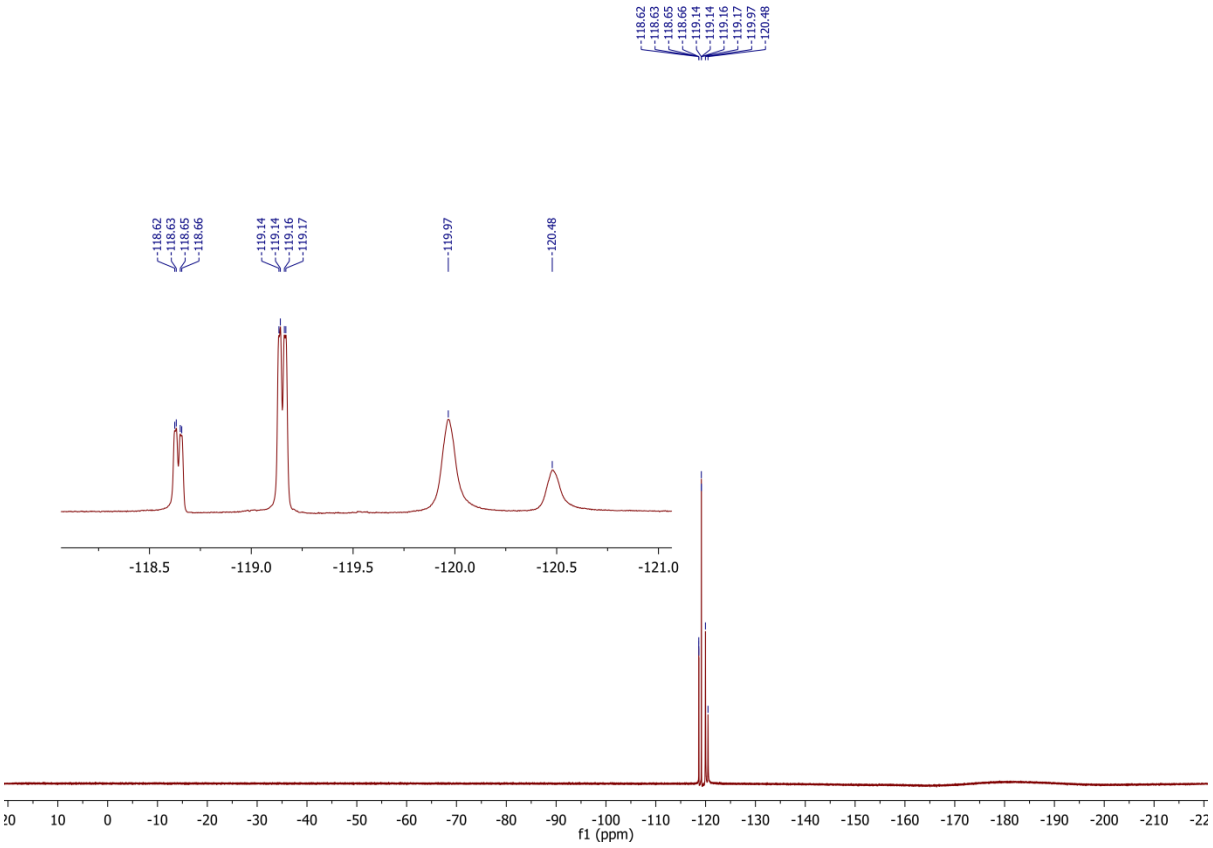


Compound **S1** ^{1}H (MeOD-d_4) and ^{13}C NMR (DMSO-d_6)

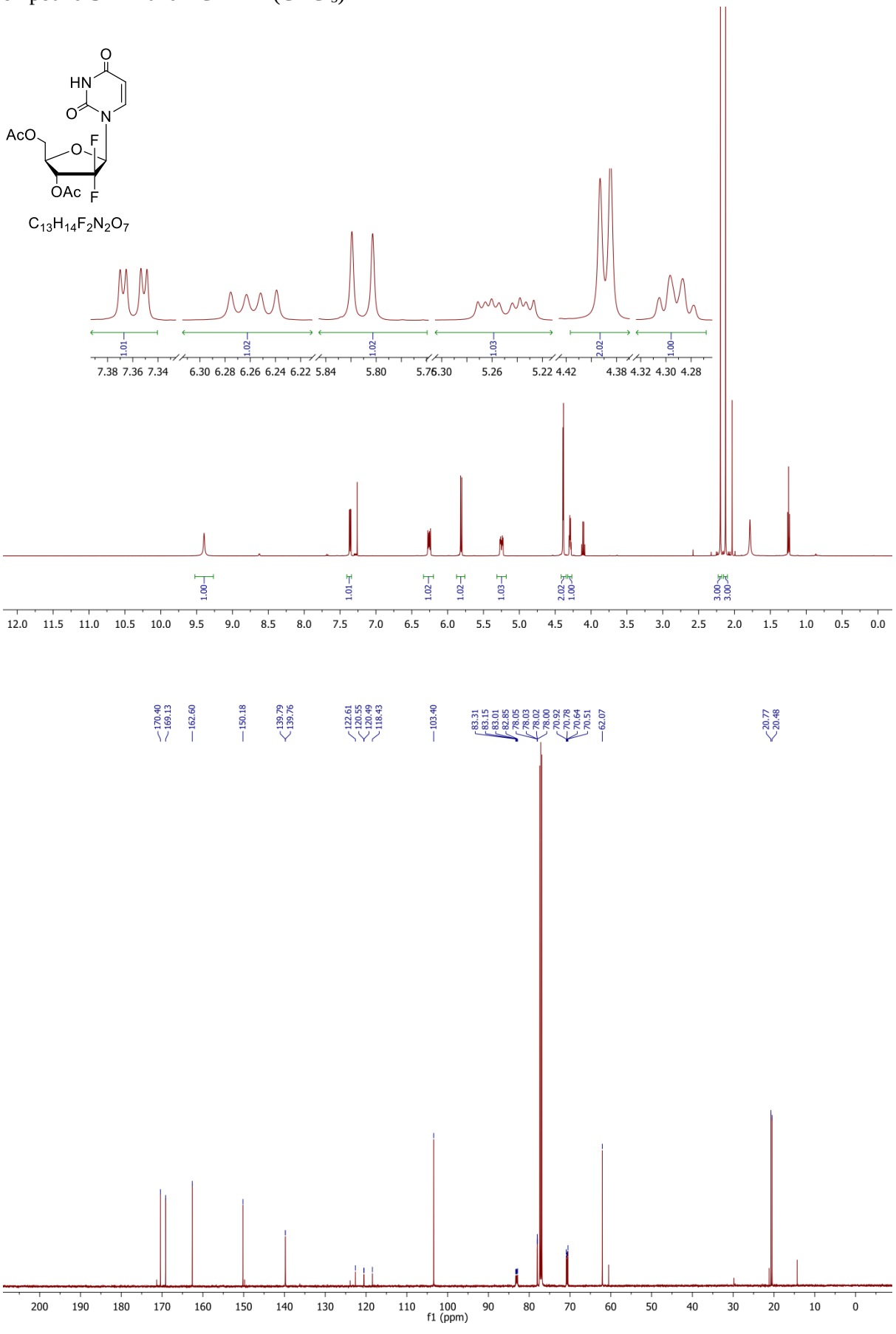




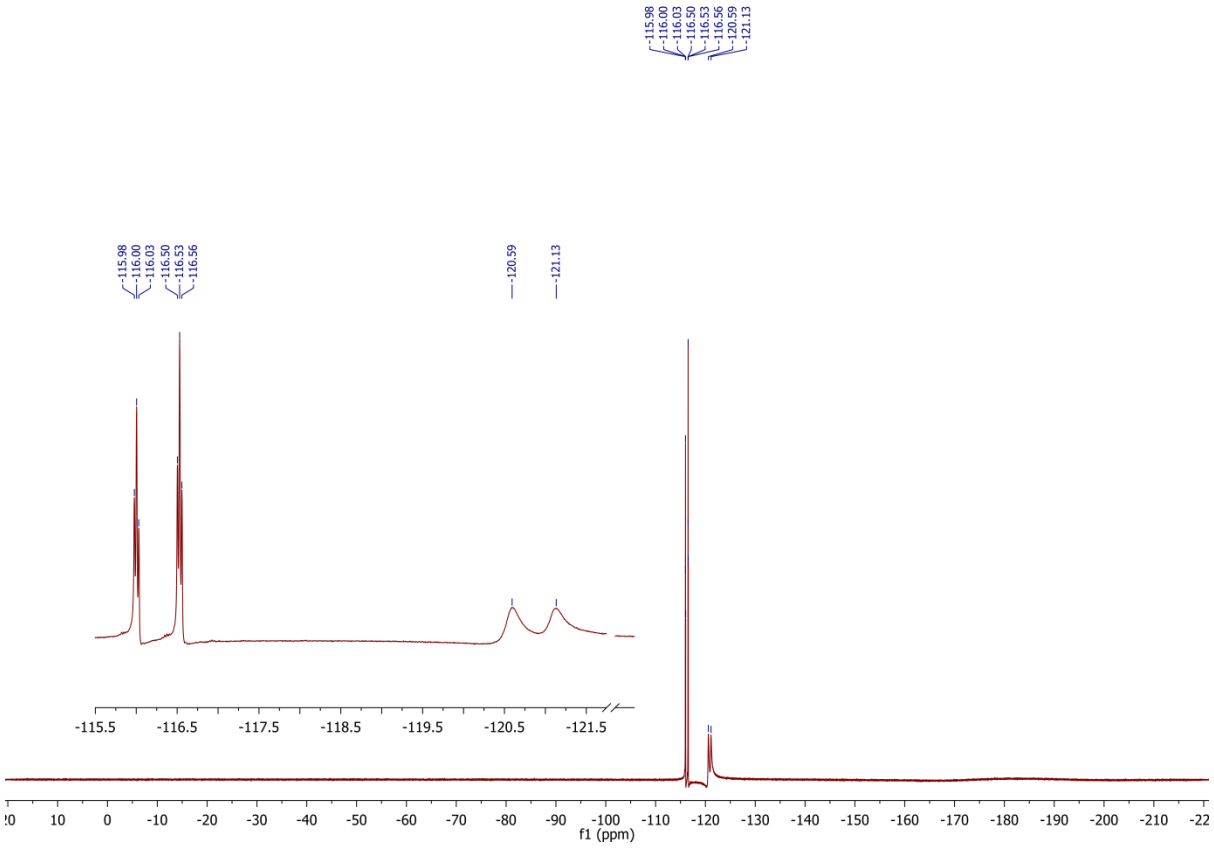
Compound **S1** $^{19}F\{H\}$ NMR (MeOD-d_4)



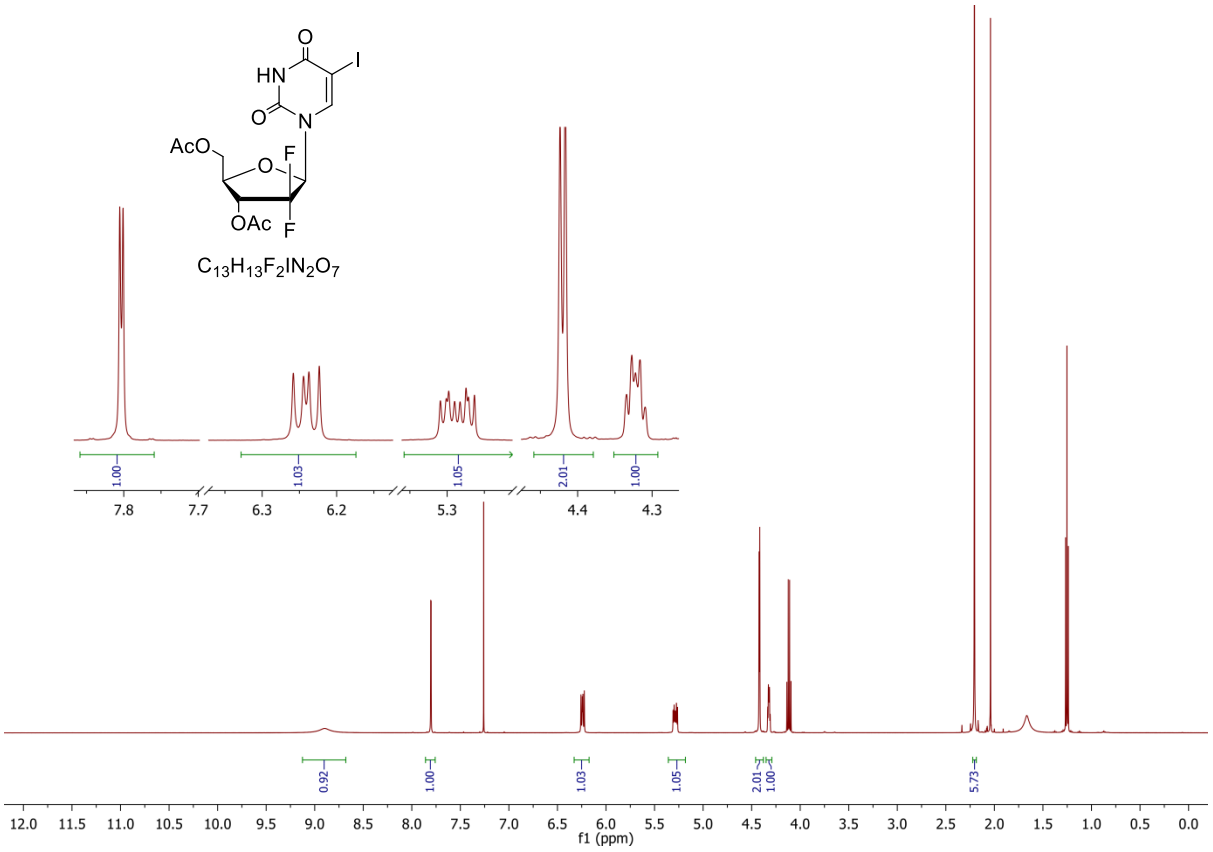
Compound **S2** ^{1}H and ^{13}C NMR ($CDCl_3$)

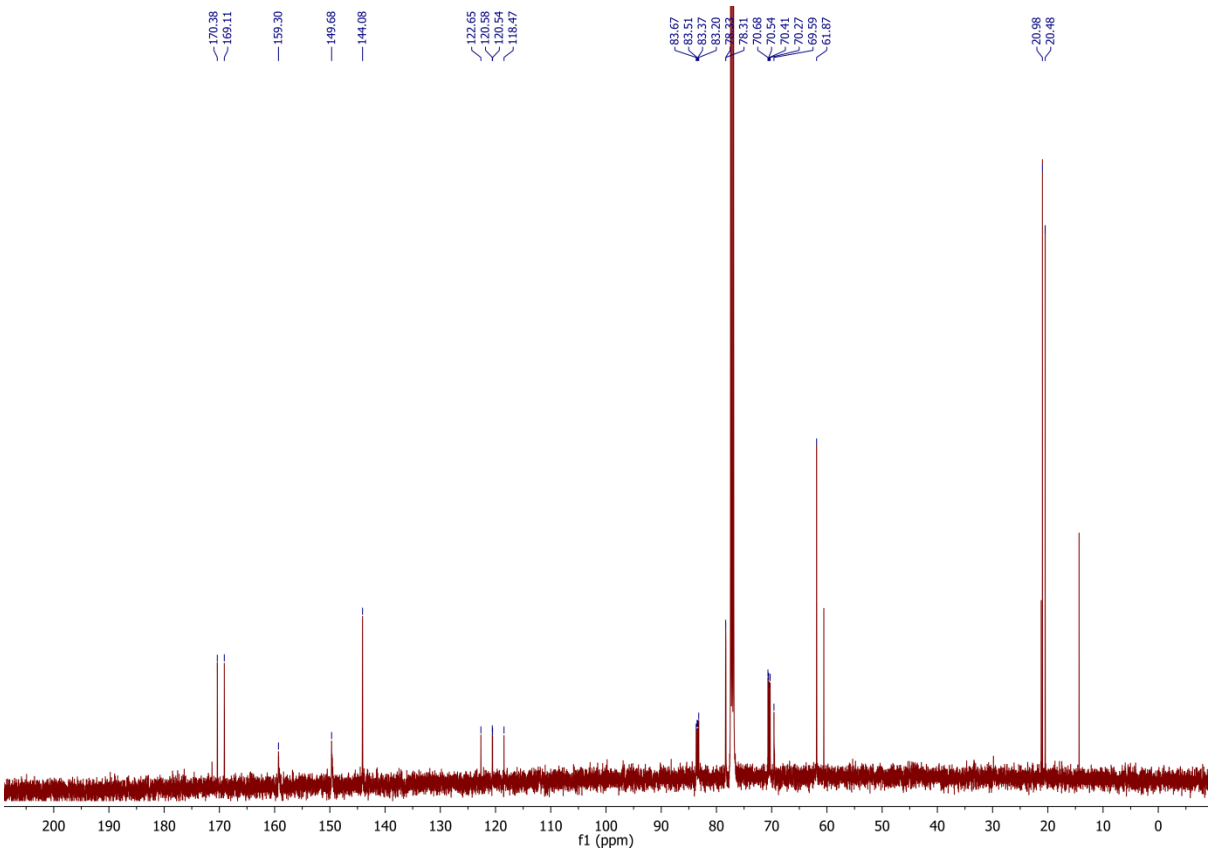


Compound **S2** ^{19}F NMR ($CDCl_3$)

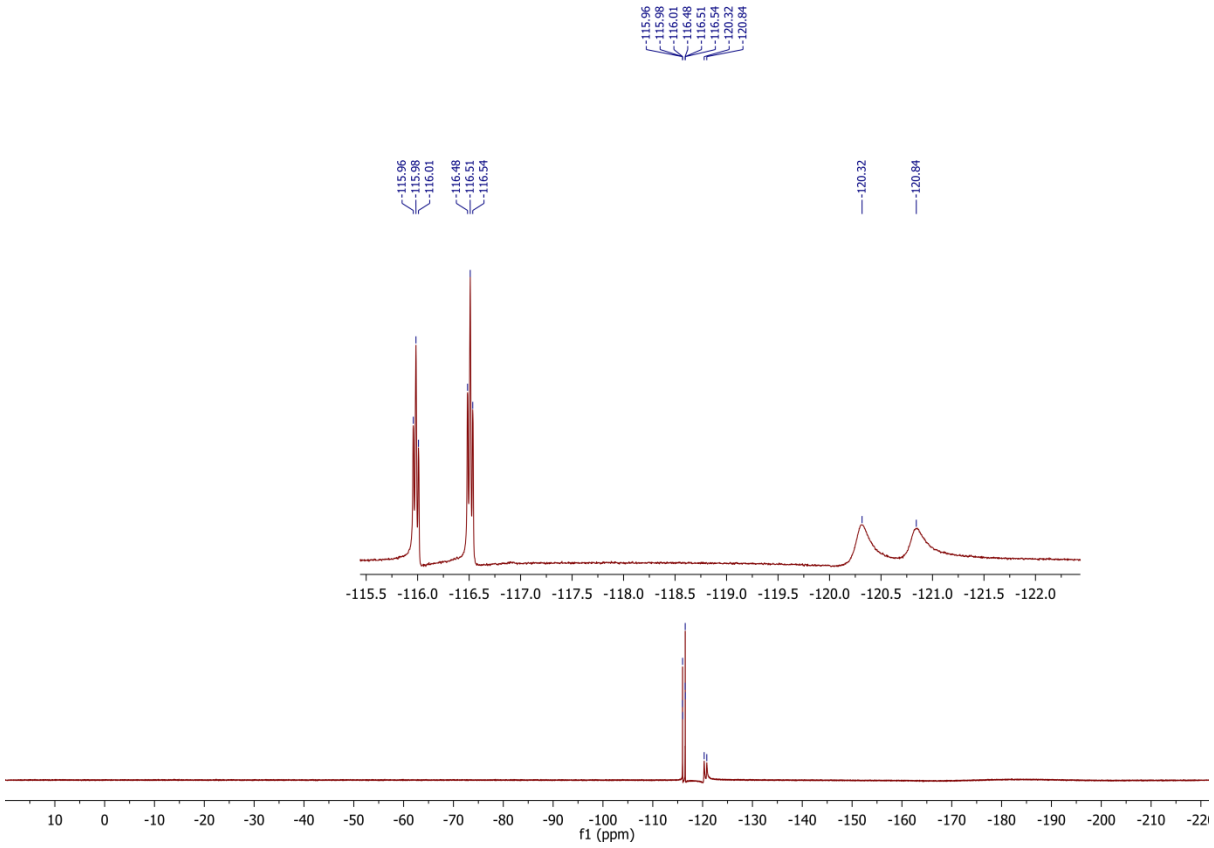


Compound **S3** ^{1}H and ^{13}C NMR ($CDCl_3$)

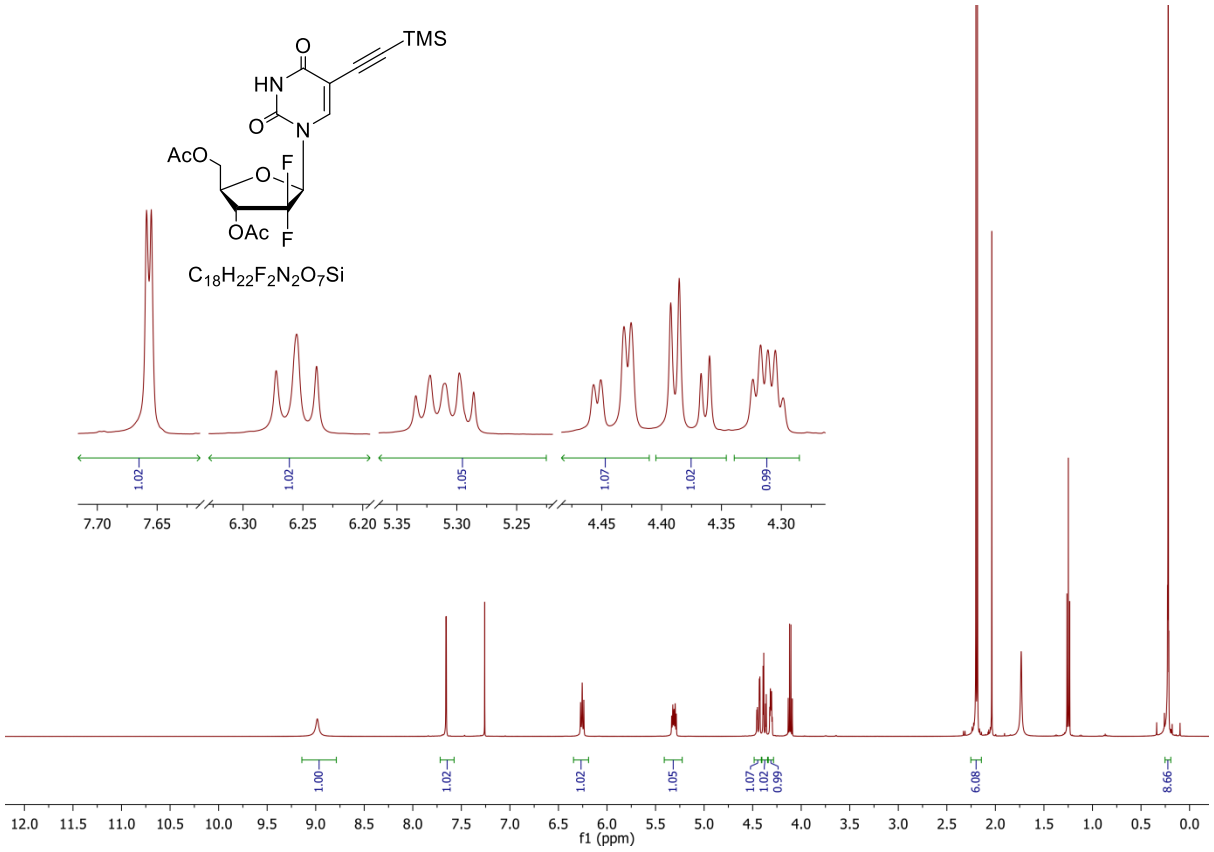


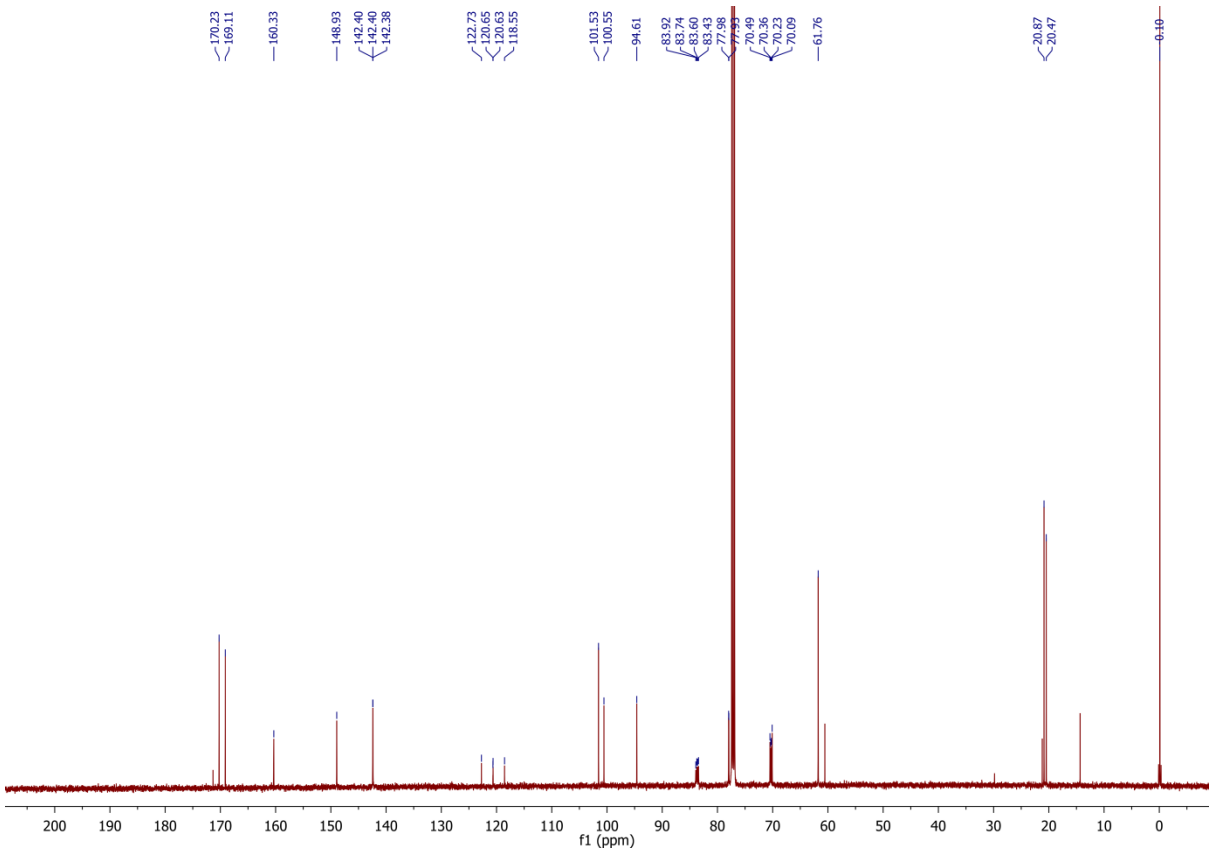


Compound **S3** ^{19}F NMR ($CDCl_3$)

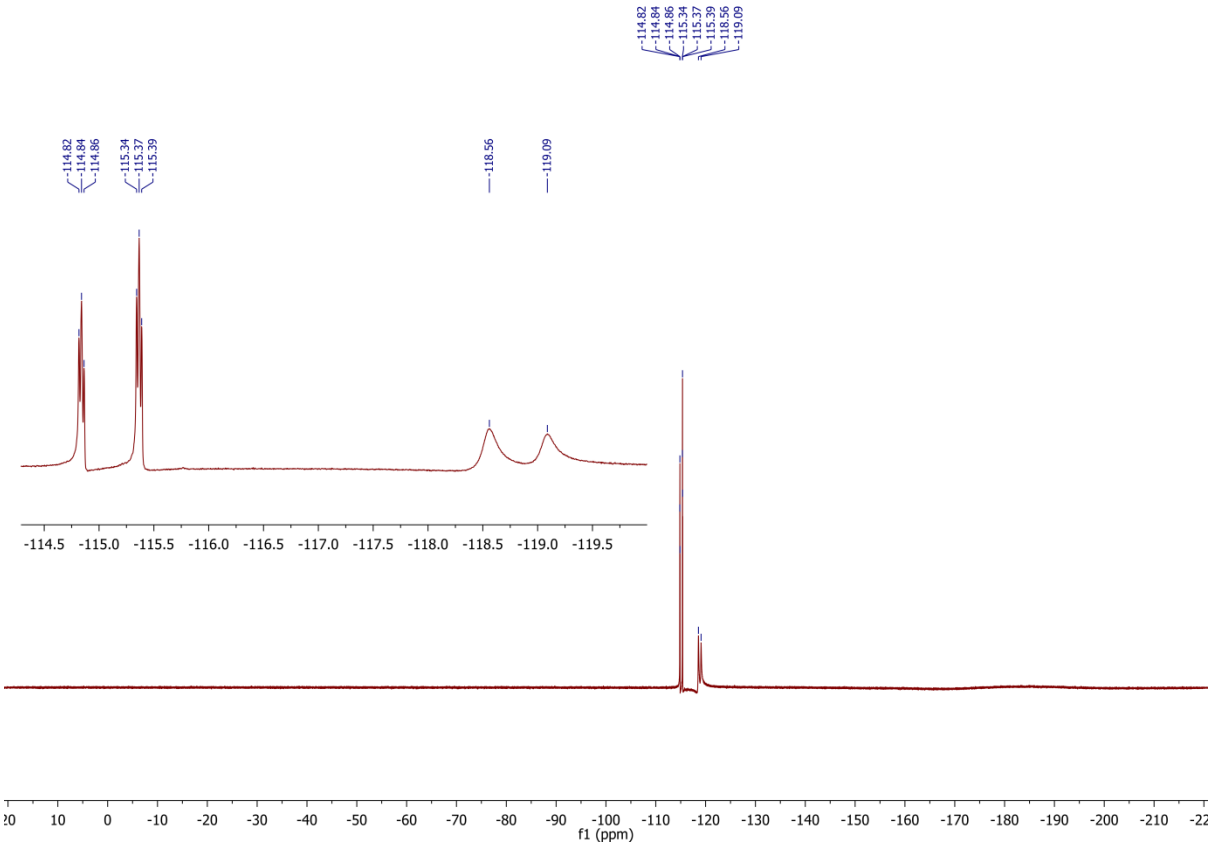


Compound **S4** ^{1}H and ^{13}C NMR ($CDCl_3$)

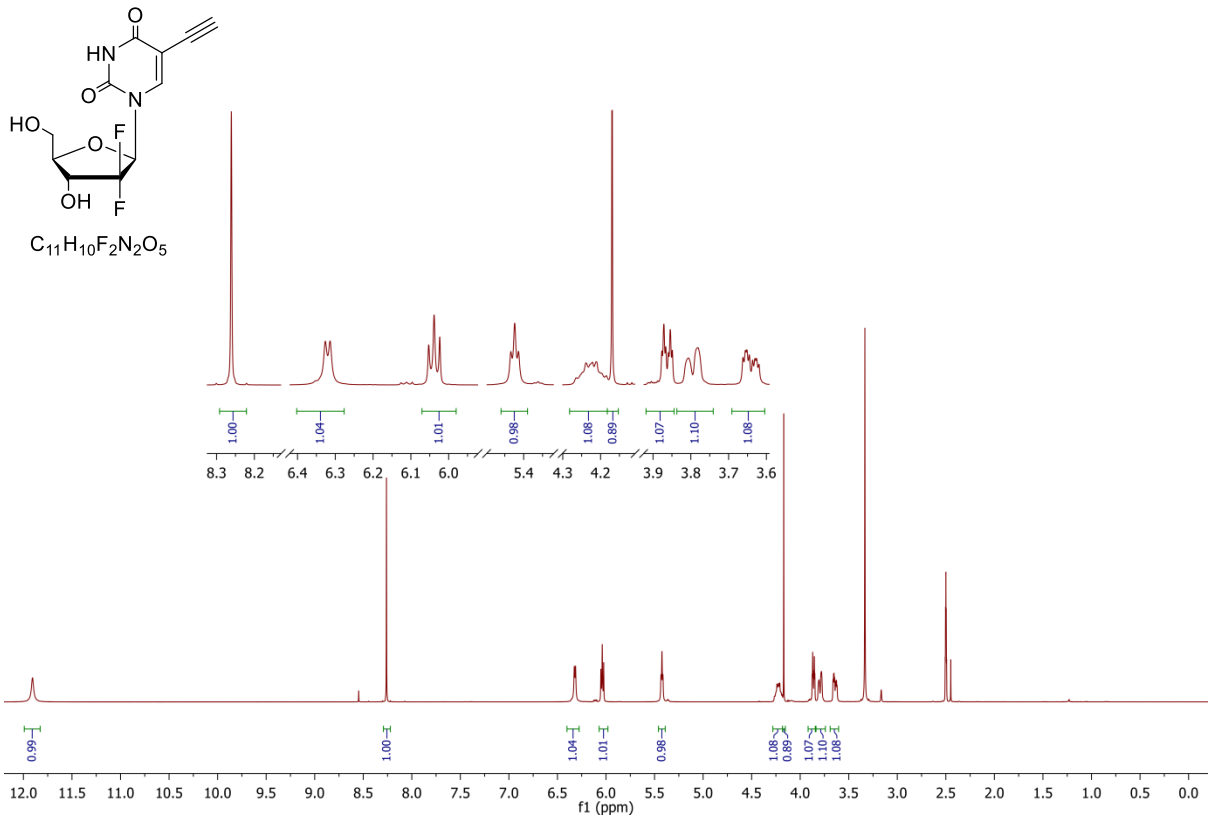


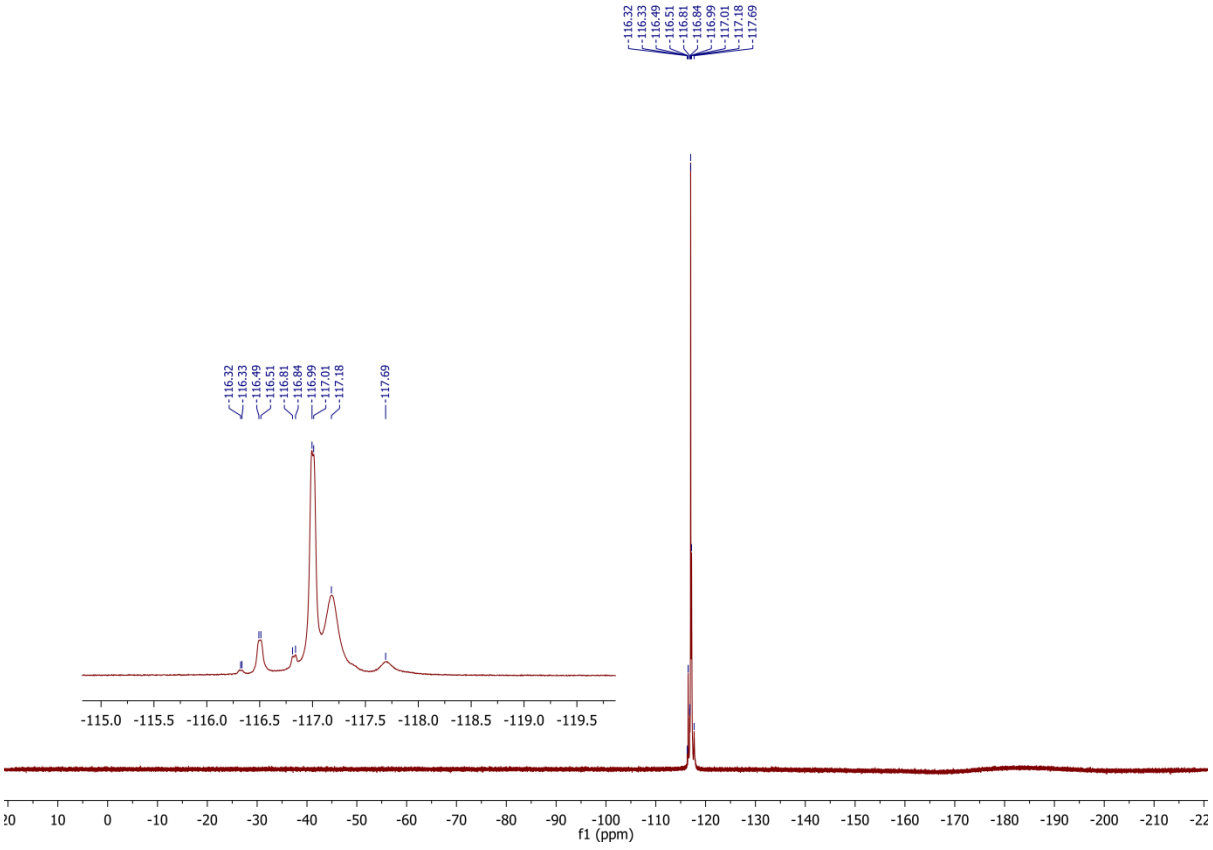


Compound **S4** ^{19}F NMR ($CDCl_3$)

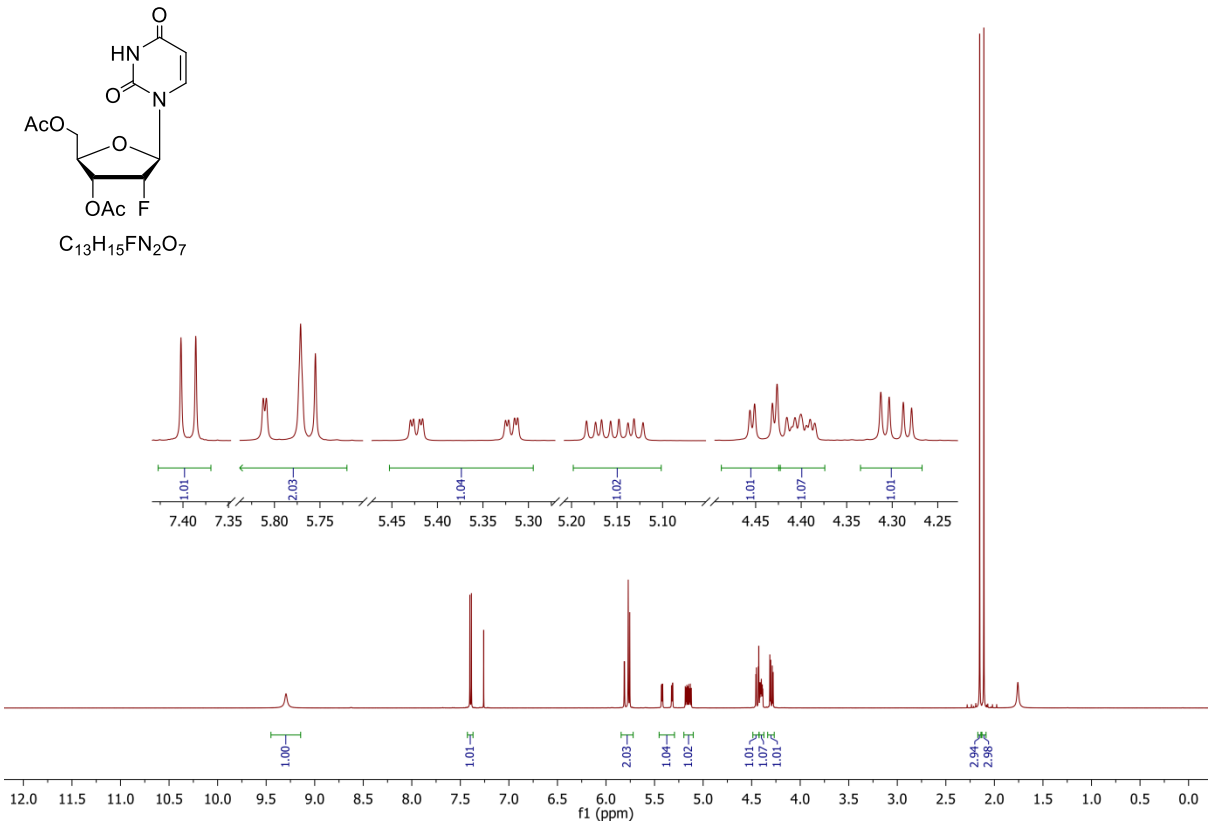


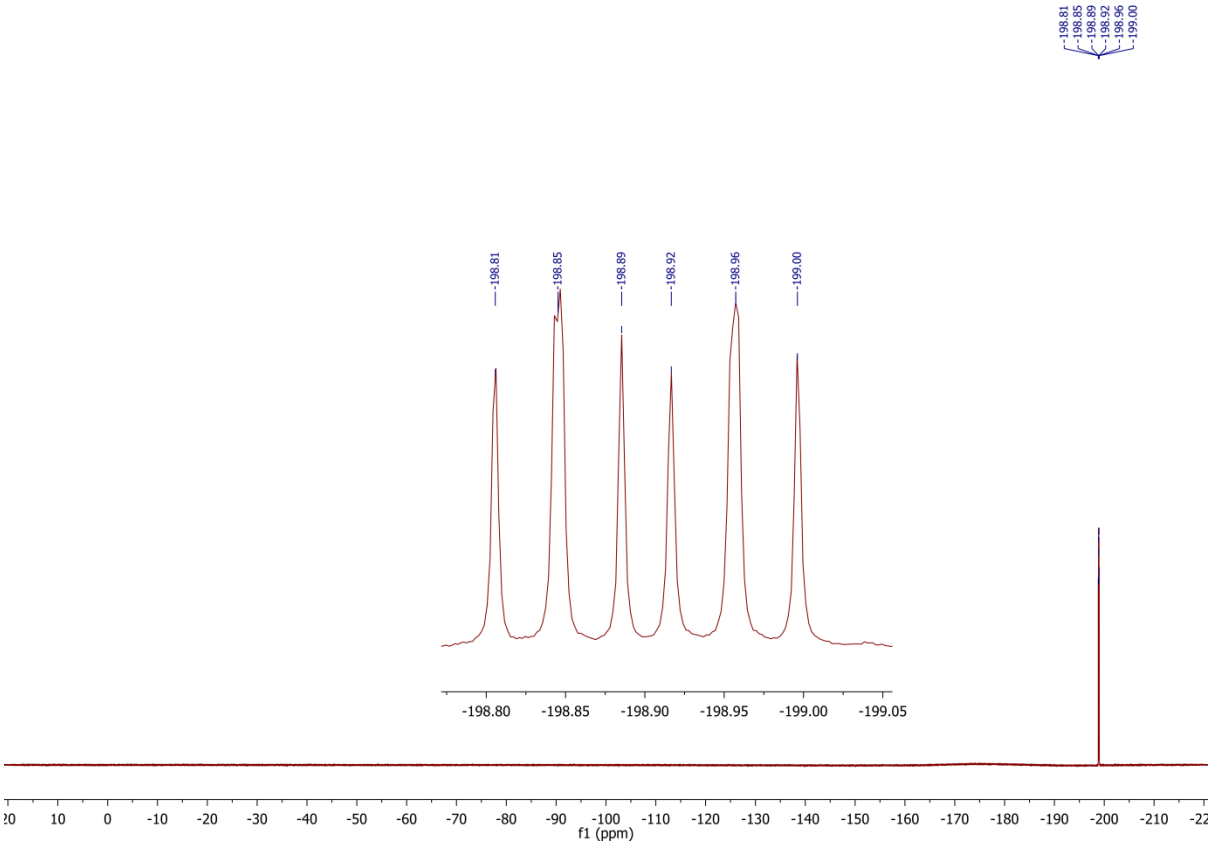
Compound **34** ^{1}H and ^{19}F NMR (DMSO-d_6)



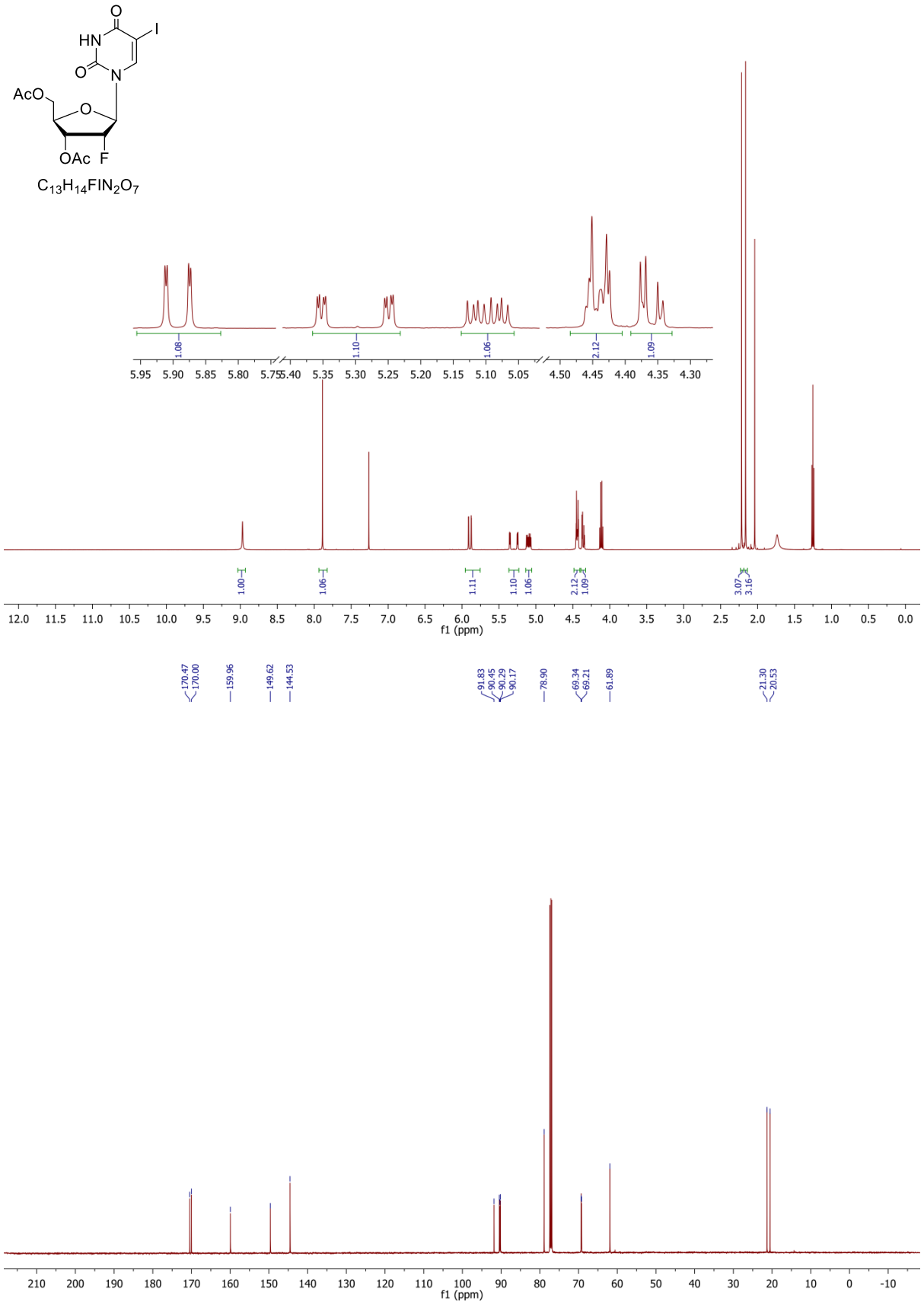


Compound **S6** ^{1}H and ^{19}F NMR ($CDCl_3$)

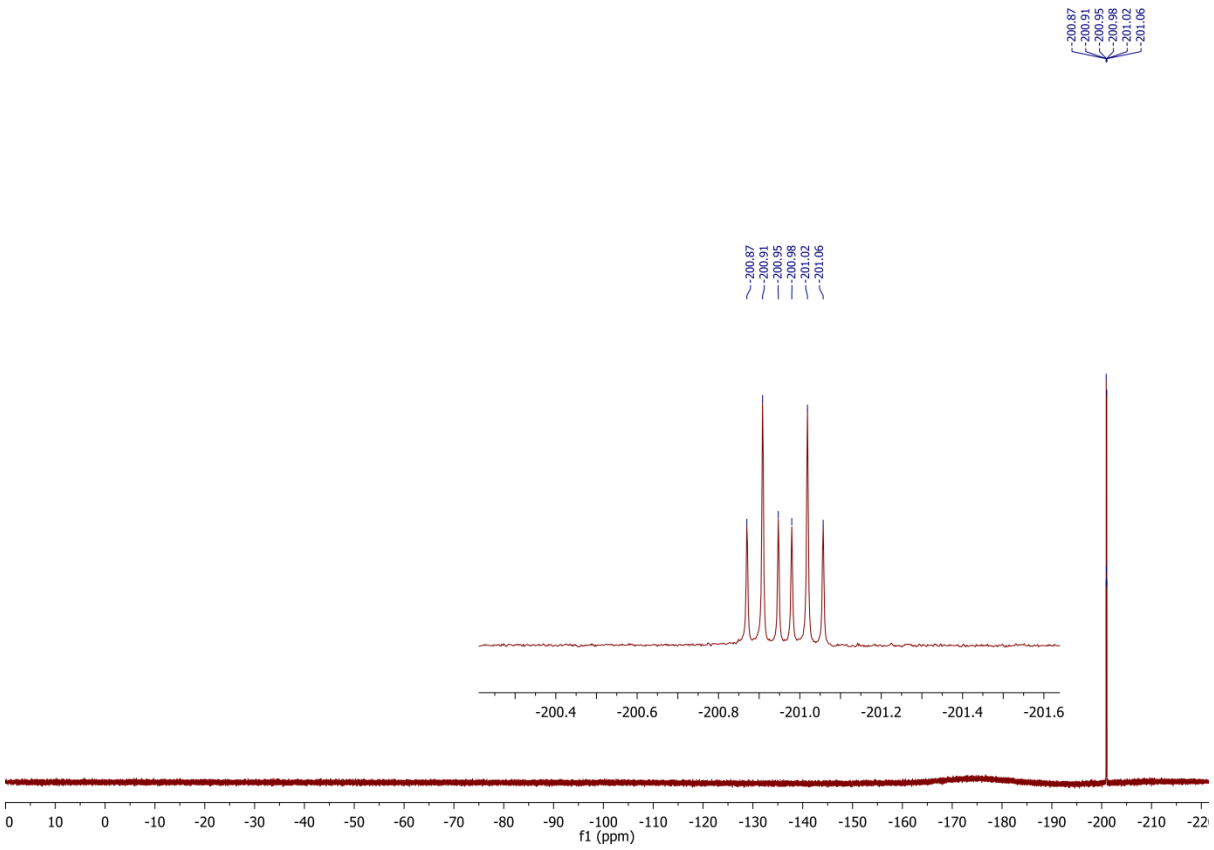




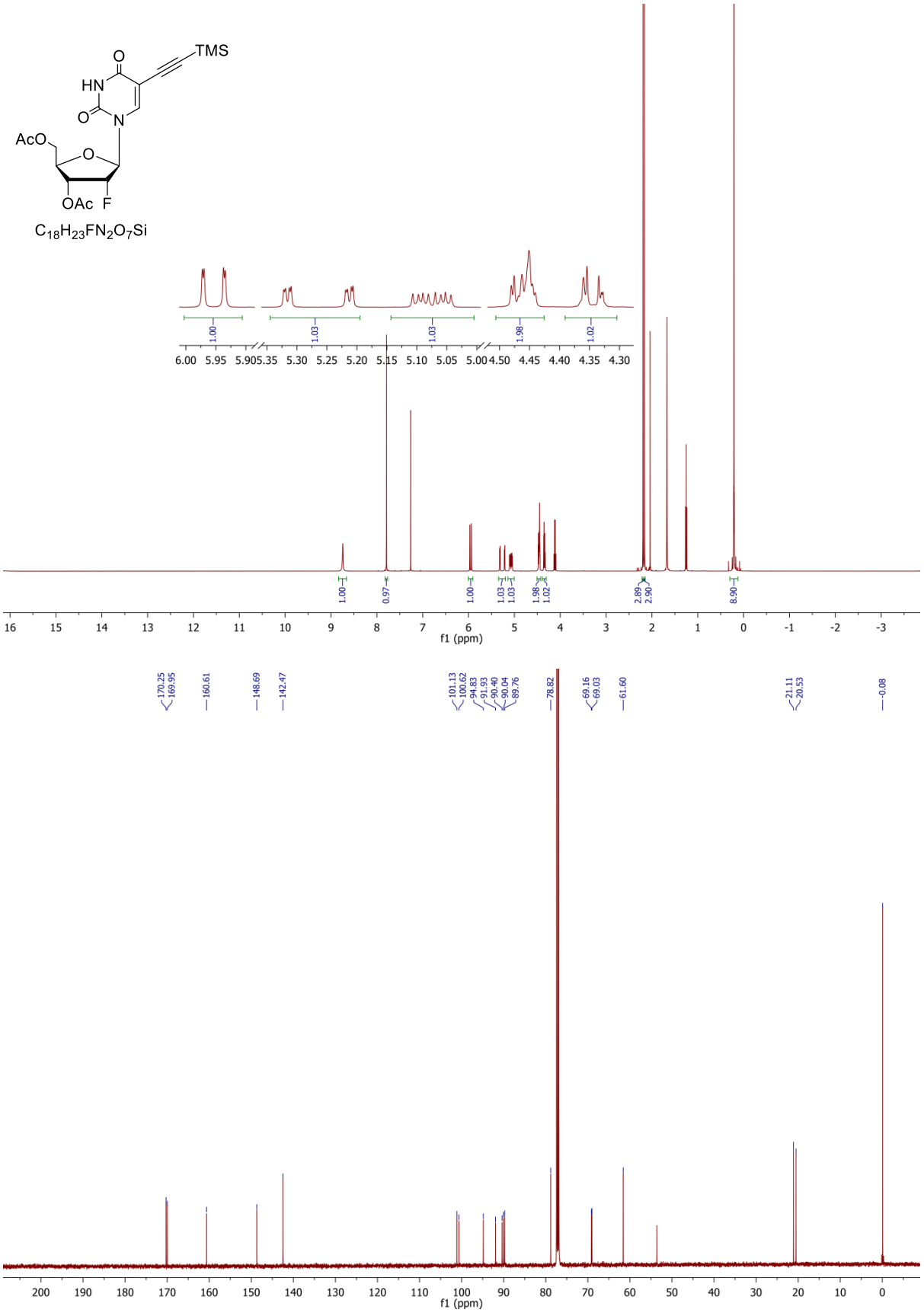
Compound **S7** ^{1}H and ^{13}C NMR ($CDCl_3$)



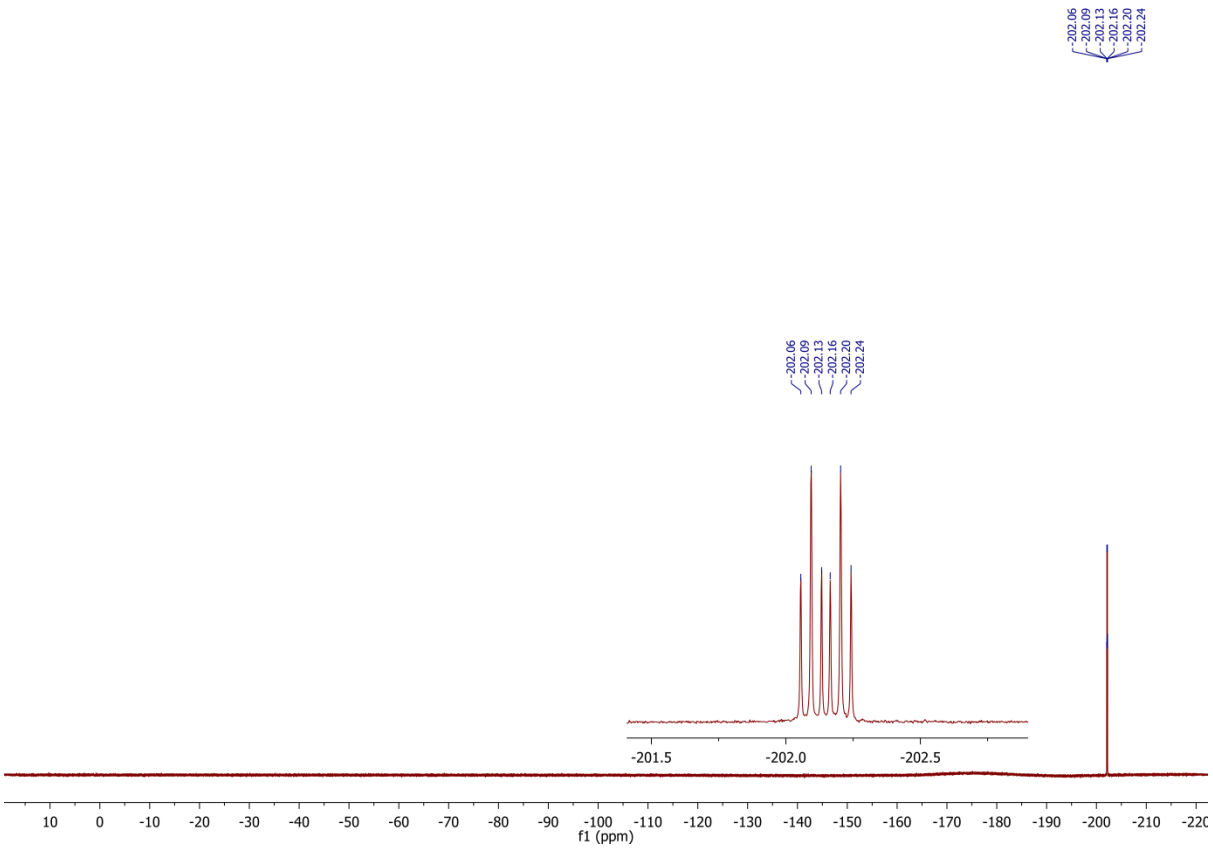
Compound **S7** ^{19}F NMR ($CDCl_3$)



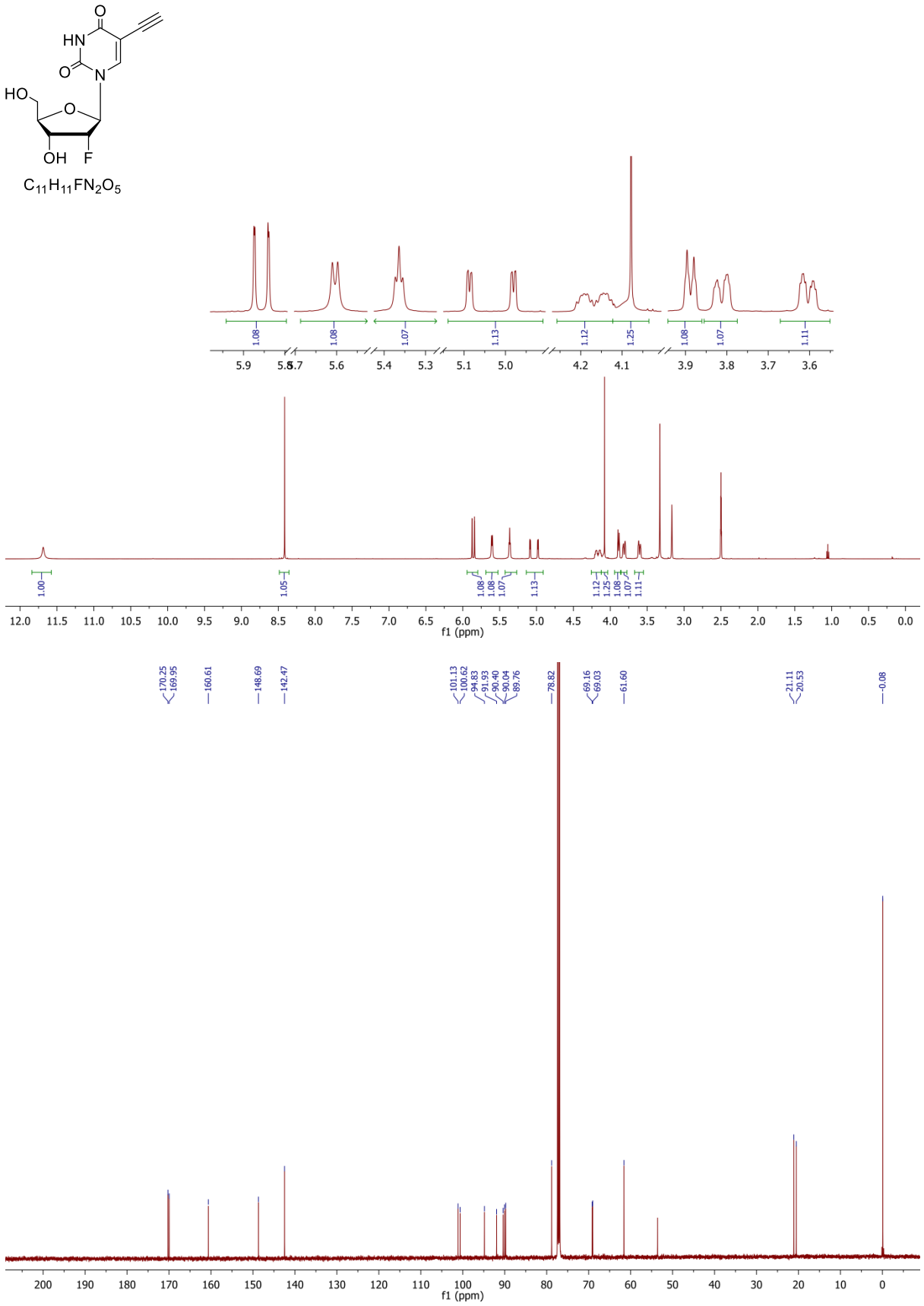
Compound **S8** ^{1}H and ^{13}C NMR ($CDCl_3$)



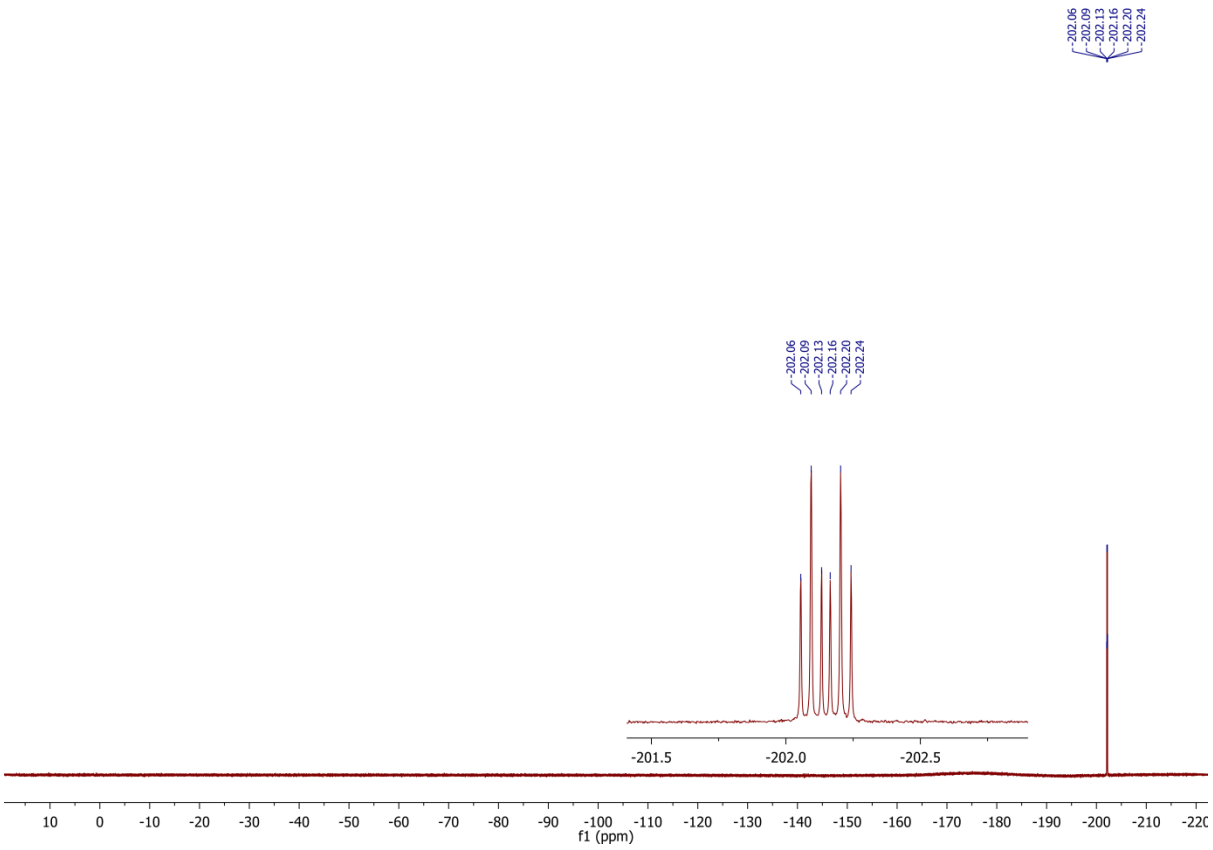
Compound **S8** ^{19}F NMR ($CDCl_3$)



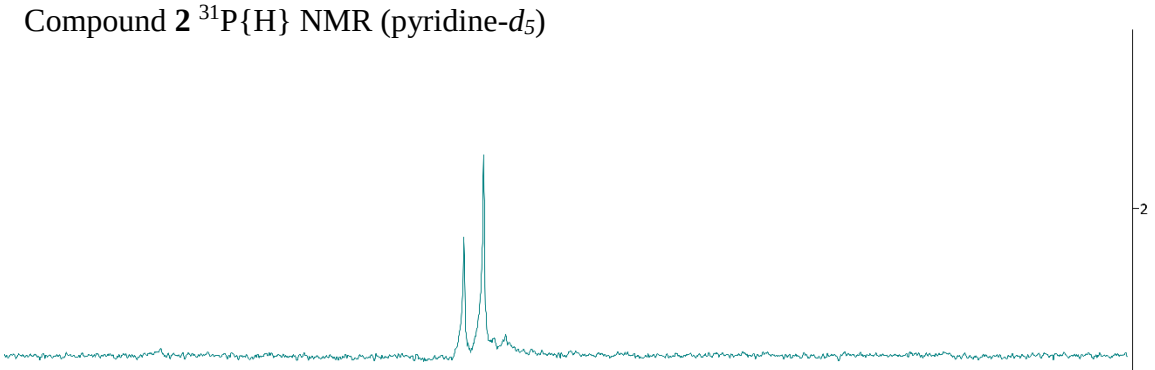
Compound **35** ^{1}H and ^{13}C NMR (DMSO-d_6)



Compound **35** ^{19}F NMR (DMSO-d_6)



Compound **2** ^{31}P{H} NMR (pyridine-d_5)



Crude reaction mixture for synthesis of **2** ^{31}P{H} NMR (pyridine- d_5)